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SUBACUTE MALIGNANT PEMPHIGUS WITH EXTENSIVE BULLAE*

(Pemphigus Subaigu malin à Bulles Extensives, Brocq)

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INTRODUCTION

Brocq, whose studies have done much to bring comparative order out of the chaos which existed in the bullous dermatoses, has recently called attention to a group of cases of pemphigus hitherto not usually separately described.[1] He has given the name subacute malignant pemphigus with extensive bullae to the condition, which he describes as closely resembling acute febrile pemphigus, but which is differentiated from it by a characteristic clinical syndrome.

While Brocq's classification of pemphigus is the one now usually accepted, there is still enough variation in the usage of the term to warrant summarizing the conditions included under it, before describing the new syndrome, and locating it in the general scheme.

Under pemphigus Brocq includes acute febrile pemphigus (pemphigus aigu fébrile grave), pemphigus foliaceus, pemphigus vegetans and chronic pemphigus (or true pemphigus). He subdivides the last into two varieties, malignant chronic pemphigus (pemphigus chronique vrai grave), and benign chronic pemphigus (pemphigus chronique vrai bénin), thus admitting into this group the few cases of apparently true pemphigus which terminate in recovery.

We are not here concerned with pemphigus foliaceus or pemphigus vegetans.

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1. Brocq, L : Schème des eruptions bulleuses. Le pemphigus subaigu malin à bulles extensives et faits connexes, Ann. de dermat et syph. Series 5 **7**:449, 1918-1919. Pemphigus subaigu à bulles extensives, in Précis-Atlas de Pratique Dematologique, Doin, Paris, 1921, P. 608. Brocq, Gougerot, Desaux et Rabreau: Pemphigus subaigu malin à bulles extensives, Bull. Soc. franç. de dermat. et syph., 1921, p. 2.

Acute febrile pemphigus is an apparently infectious disease characterized by a sudden onset and intense febrile reaction, an eruption consisting solely of serous or hemorrhagic bullae and by a fatal termination within one to three weeks, recovery being rare. It is seen almost entirely in butchers and in those who handle cadavers of animals. It is probably an acute infectious disease.

Chronic pemphigus is usually of insidious onset, is characterized by a widespread monomorphous bullous eruption which arises rapidly without evidence of inflammation of the skin, which is attended with little or no pain or pruritus, which affects the whole body and in which the bullae are reproduced in successive crops. The mucous membranes are frequently affected early in the disease. There is a fatal termination within a few months to a year, but there are frequently intermissions in the progress of the disease, with temporary improvement.

SUBACUTE MALIGNANT PEMPHIGUS

Brocq describes subacute malignant pemphigus as a syndrome presenting the general appearance of a severe infection without high temperature but with marked prostration of the patient who remains in bed without moving, immobilized by the severe pain which occurs on the surface of the excoriations whenever motion is attempted, speaking only with great difficulty on account of the lesions of the throat, of the soft palate, of all the buccal mucous membrane and that of the lips, lesions which are superficial but extremely painful.

In its evolution this syndrome is characterized by its frequent origin on the mucous membrane and in its objective appearance by the perfectly characteristic aspect of the cutaneous lesions which, on the site of the broken bullae, rapidly develop denuded, moist, sanguinolent surfaces which show no tendency to heal and which extend progressively at the edges with detachment of the horny layer of the skin.

This peripheral extension, simulating that of an extremely virulent impetigo, without tendency toward cicatrization in the center of the lesion, together with the gravity of the general condition in spite of only moderate fever and the suffering experienced by the patient, appear to him to establish a characteristic syndrome which gives this clinical picture an individual aspect, and which permits its immediate differentiation not only from dermatitis herpetiformis and dermatite polymorphe but also from all other bullous diseases. It also permits a bad prognosis. In the last twelve years Brocq has seen several such cases, six of them terminating in a relatively rapid death. There were two patients who either recovered or disappeared from observation greatly improved, but in these two cases the bleeding surfaces following the rupture of the bullae were not large, and the peripheral extension was slight.

Brocq's description of the syndrome just quoted is sufficiently detailed to obviate the necessity of summarizing the cases he reports.

We have recently had the opportunity of studying a patient who presented a typical picture of this syndrome.

History.—M. B., No. 78669, 69 years of age, was a widow born in Italy. She was admitted to the New Haven Hospital on Dec. 29, 1920, complaining of painful sores on her chest, abdomen and back. These had started six weeks

Fig. 1.—Early appearance of lesions.

before as small vesicles on her sides, back and neck, which had rapidly increased in size and number. She had had no previous illnesses of any consequence. She had had ten children, three of whom were alive and well, and seven had died between the ages of 5 months and 6 years.

Examination.—The physical examination revealed nothing of consequence except a slight soft systolic murmur at the aortic area and slightly sluggish pupils. She had no teeth. Blood examination on Dec. 30, 1920, showed hemoglobin 80 per cent. white blood corpuscles 22,600, polymorphonuclears 81 per

cent., small mononuclears 16 per cent., large mononuclears 3 per cent., eosinophils 0, basophils 0. A blood culture taken Dec. 31, 1920, showed no growth. A second culture taken Feb. 9, 1921, was also negative. Cultures from the bullae were not made because there was no possibility of obtaining uncontaminated material. The Wassermann reaction on Dec. 31, 1920, was negative with alcoholic antigen and + with cholesterinized antigen. The urine during her stay in the hospital was negative, except that an occasional specimen contained a faint trace of albumin. The temperature ranged between 98 and 102 F. and was usually about 100. Within the two weeks previous to her death it reached 103 once or twice. It was about 100 just before death.

Fig. 2.—Later appearance of lesions.

When the patient was admitted to the hospital her chest and back were covered with lesions varying in size from that of a silver dollar to that of the palm. These lesions were all covered with thick, partly dried, yellow crusts which had formed on the sites of previous bullae which had received no attention. Their appearance on the chest, where they were largest, resembled that of a severe neglected impetigo in a debilitated subject. On the back they more closely resembled the usual lesions of chronic pemphigus, as is shown in Figure 1. There were no lesions in the mouth. A few days after the crusts had been carefully removed the lesions presented smooth, red, moist denuded areas

which rapidly extended at the borders by elevation of the epidermis. There was slight inflammatory reaction at the edges. Only in a few lesions was there at any time any evidence of a tendency to heal, and the lesions increased in number and size and became confluent until nearly the whole of the chest and upper part of the back was denuded, as is shown in Figure 2. The appearance of the lesions was so like that of those in one of the cases reported by Brocq that his description may be quoted verbatim for our patient.

"There was a strikingly characteristic appearance of the bullae on the presternal region and about the middle of the back. These bullae, which had appeared several weeks before, had broken, leaving the corpus mucosum and the derma exposed as if a vesicatory had been applied, and far from showing any cicatrization, they were extending at their edges by detaching the epidermis which was raised at the periphery in large shreds. They thus formed large

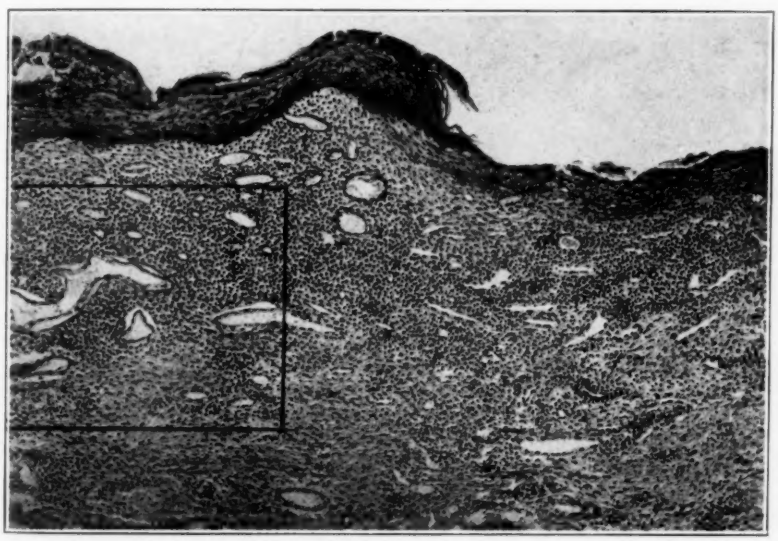

Fig. 3.—(Low power photomicrograph retouched). Margin and base of bleb, showing dilated vessels, diffuse cellular reaction and absence of regenerative activity on the part of the epidermis.

surfaces which, because of the confluence of several lesions, were irregular. The surfaces were raw, oozing, slightly hemorrhagic and very painful."

There were a few small lesions on the upper part of the arm. Except for these there were none on any part of the body except the trunk. The abdomen was not affected. A few days before death a few superficial, and not very painful lesions, appeared on the buccal mucous membrane.

Clinical Course.—During her stay in the hospital the patient continually complained of the painfulness of the lesions on the skin. She was at first not particularly prostrated. There was no marked change in her condition until three or four days before her death when the prostration became much more marked. On Feb. 24, 1921, there was a sudden profuse hemorrhage from the mouth, the source of which was never determined, and on Feb. 25, 1921, she died.

During the two months that she was under our observation various soothing applications were applied with no alleviation of the pain and with no effect on the lesions. Sodium cacodylate was given hypodermically for about two weeks with no effect.

The most striking clinical characteristics were: the extent and painfulness of the lesions, the absence of tendency toward healing, the localization on the trunk, the absence of lesions in the mouth till late in the disease, and the moderate amount of fever.

One of Brocq's patients had only a few lesions in the mouth. Perhaps the absence of teeth in our patient may have partially accounted for the lesions being so few.

No biopsy was made, but permission for a necropsy examination was obtained.

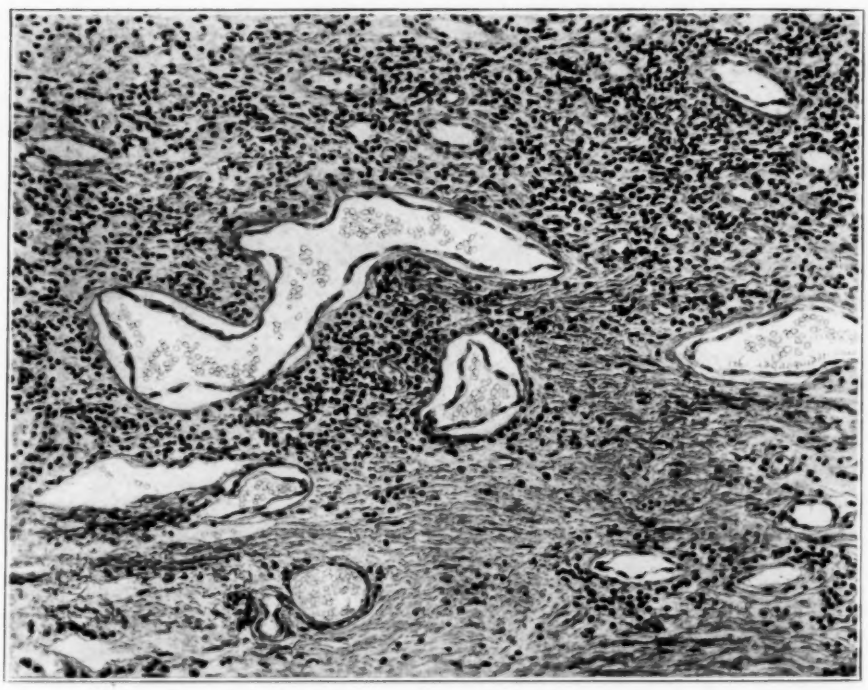

Fig. 4.—Higher magnification of an area in Figure 3. The prominent endothelial lining of the blood vessels and the mononuclear character of the infiltrating cells are well shown.

Necropsy Examination.—The skin lesions, which constituted the most striking gross feature, have already been fully described. It may be added, however, that in removing blocks of skin for histologic study, the superficial character of the lesions could be well demonstrated. The exfoliated tissue seemed to have included only the epidermis. This was clearly so in the case of the denuded patches on the anterior surfaces of the thorax and arms, on which the lesions were quite dry. The exposed derma here was bright red, but strikingly smooth and free from granulations. Over the back there was considerable seropurulent discharge from the raw surfaces and some undermining of the skin edges,

suggesting a more active secondary bacterial infection in the dependent and less protected regions.

The subcutaneous tissues and indeed the tissues in general were unusually dry, and there was little fluid in the stomach and intestines and practically no urine in the bladder (a condition referable no doubt to the painful mouth lesions and the resulting diminished fluid intake).

The gross changes in the thoracic and abdominal viscera were not striking or important, and may be briefly summarized:

There was a general atrophy of the organs of the senile type. The heart weighed only 225 gm. and its musculature was quite dark ("brown atrophy"). The liver and spleen were likewise abnormally small, the former weighing 1000, the latter 38 gm. The kidneys were slightly reduced in size and showed occasional arteriosclerotic scars and several small cysts. There was a moderate

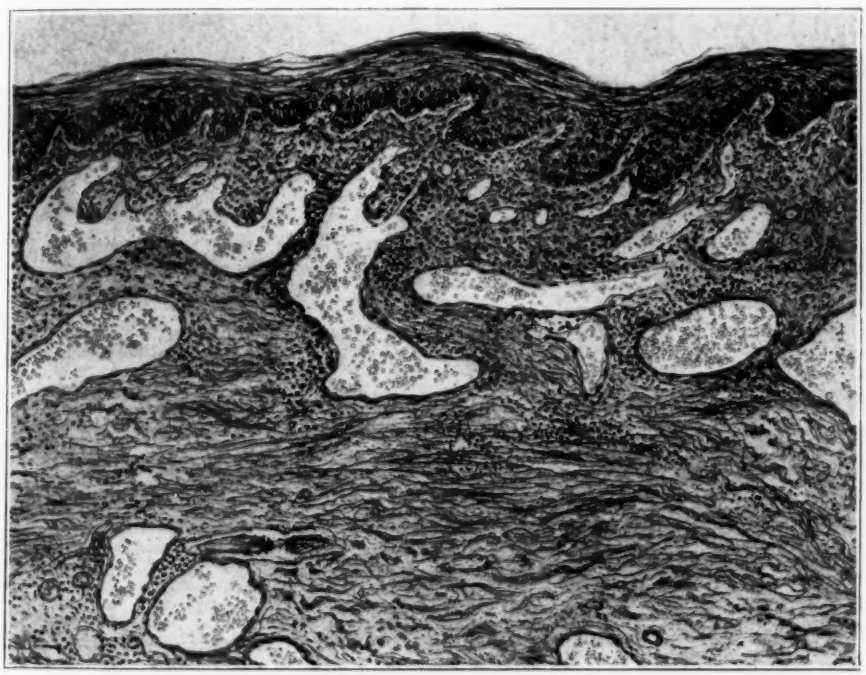

Fig. 5.—(Low power photomicrograph retouched). Intact skin in neighborhood of bleb. The vascular spaces in corium are even more prominent than in the exfoliated areas, but the cellular reaction is less marked. Note the narrow pale fatty zone just beneath the epidermis.

generalized arteriosclerosis. The most marked changes were seen in the respiratory tract. The mucosa of the larynx, trachea and bronchi was reddened and, in the trachea particularly, it had lost its normal lustrous translucency and was quite opaque. There was throughout more or less mucopurulent exudate. Scattered through the lungs were small firm, red patches, the picture of an early hemorrhagic bronchopneumonia.

Microscopically, the only noteworthy findings were in the skin and upper respiratory tract. Skin: A number of sections, including the exfoliative lesions

on the thorax, arms, thigh and adjacent normal looking skin, showed practically the same picture. The most striking feature was the presence of numerous dilated, thin walled blood vessels throughout the corium. These vascular spaces were seen not only in the areas in which the epidermis was lost, that is, the base of the blebs, but extended for considerable distances marginally beneath an intact and apparently only slightly altered epidermis. The size and frequency of these dilated vessels and their relation to the epidermis are well shown in Figures 3 and 5. In places the dilatation was even more marked than these illustrations show.

The endothelial lining of these blood spaces was quite prominent (Fig. 4), so much so that some of the smaller vessels resembled epithelial-lined ducts.

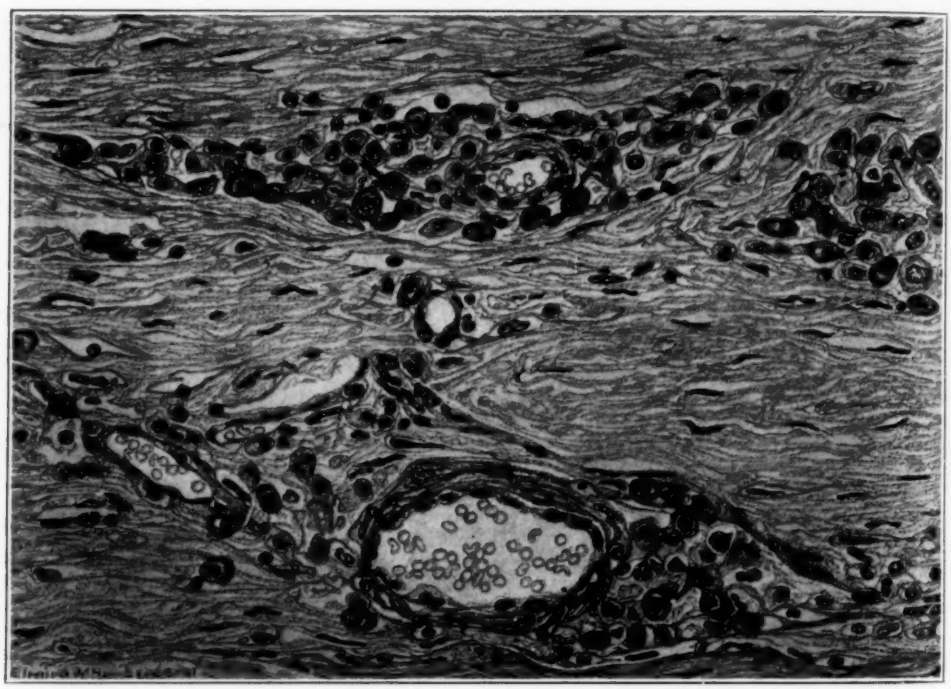

Fig. 6.—(High power drawing). Perivascular infiltration in deeper zone of corium. The cells here as elsewhere are mostly of the plasma cell type.

Fresh fluid blood filled practically all of the spaces. In a few of these just beneath the denuded surface, there was a homogeneous pink staining coagulum, but no definite thrombi were demonstrable.

The second significant feature of the cutaneous lesions was the cellular reaction. There was everywhere more or less round cell infiltration. The cells showed a tendency to a definite perivascular grouping, but in the base of the blebs they were scattered diffusely. The cells varied in type, but the dominant cell was of the plasma cell type (Fig. 6) having a fairly dense round nucleus, somewhat excentrically placed, and a relatively large amount of deeply staining cytoplasm (hematoxylin—eosin preparation). There were a few small lymphocytes and a considerable number of the mononuclear cells of a rather

indifferent type, with vesicular nuclei and irregular pale-staining cytoplasm. No polymorphonuclear leukocytes were seen except in the detritus forming the base of the bleb, and they were scarce even here. Eosinophils, which are rather regularly present in both acute and chronic pemphigus, were rarely seen. There were indeed a few large mononuclear cells which showed a distinct acidophilic and more or less granular cytoplasm, but these were apparently large mononuclear phagocytes which had engulfed red blood cells, and not true eosinophils.

Changes in the connective tissue of the corium were not pronounced. There was relatively slight edema, no evidence of degeneration, and very little proliferative reaction. Fibroblasts were seen here and there, mostly near the denuded surface, but there was not such active proliferation as is commonly associated with ordinary bacterial or chemical injuries of the skin of similar grade, and

Fig. 7.—(Low power photomicrograph, retouched). Acute and subacute inflammatory reaction in trachea. Mucosa is partially exfoliated with an exudate of polymorphonuclear leukocytes, serum and red blood cells in the superficial zone. Changes in the deeper zone are shown in Figure 8.

there were no budding capillaries. In other words, a true granulation tissue was absent.

The changes in the epidermis were variable. At the margin of the bullae the epidermal layer ended rather abruptly. In some places the free edge was lifted up for a short distance by what was obviously fluid accumulation. There was little evidence of epithelial proliferation. Except near the margins of the blebs, the epithelium showed only moderate degenerative changes, swelling and vacuolization. In general, regressive changes were more marked in the lower layer of the rete mucosum. There was no vesicle formation within the epidermis itself and no cellular infiltration except at the bleb margin.

The papillae were in general flattened and just beneath the basal layer of the rete there was a narrow but well marked fatty reticular zone (Fig. 5). It

seemed possible that this change in the uppermost portion of the corium might represent the first stage of bleb formation, though this is not clear. The epidermis in general was thin, in places only four or five cells thick. This was no doubt a part of the senile atrophy of the tissues and was probably not related to the existing disease.

There was little or no reaction about the sudoriferous glands and the occasional hair follicles, and the nerve bundles were apparently everywhere uninvolved.

Respiratory Tract: Sections of the trachea and bronchi showed evidence of both an acute and a subacute or chronic inflammatory process (Fig. 7). Here and there the epithelial lining was lifted up by serum, and in places there was widespread desquamation. Bacterial stains showed numerous gram-positive

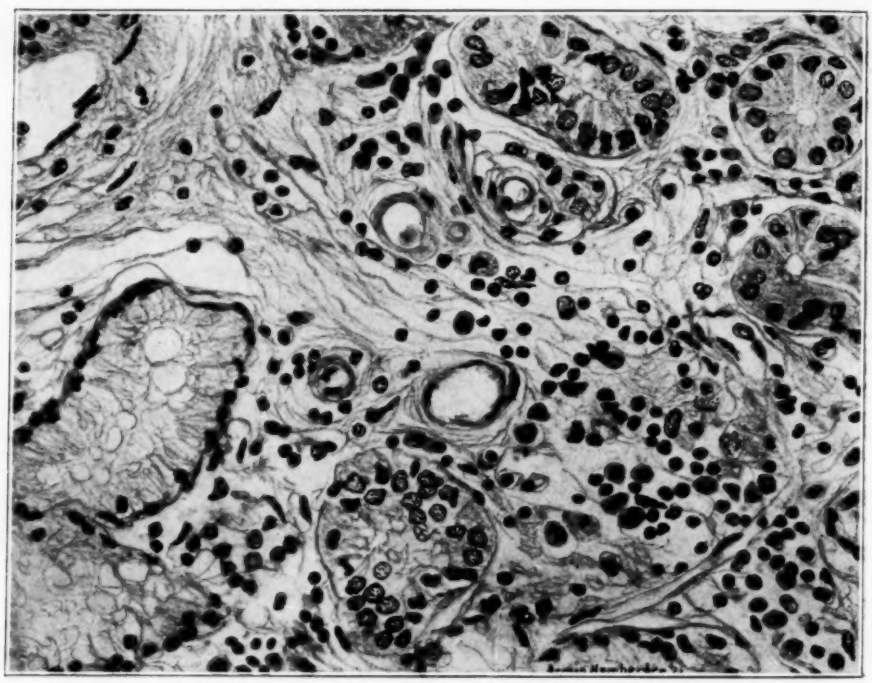

Fig. 8.—Higher magnification of an area in Figure 7 showing edema and mononuclear reaction about the mucous glands. Many of the cells are of the same type as those in the cutaneous lesions.

cocci entangled in the cilia and scattered through the submucosa. Polymorphonuclear leukocytes, fibrin and red blood cells constituted the exudate along the surface and in the superficial layer of the submucosa. In the depths of the submucosa, especially about the mucous glands, there was an infiltration by mononuclear cells, mostly of the plasma cell and lymphocyte types, and edema (Fig. 8). Connective tissue proliferation was slight. This combination of acute and subacute reaction obtained throughout the bronchial tree. In the lungs, there was about the smaller bronchi a patchy exudate into the alveoli, consisting chiefly of red blood cells and polymorphonuclear leukocytes, obviously a terminal process.

DISCUSSION

The histologic picture of the cutaneous lesions in this case correspond in general to that of chronic pemphigus as described by previous investigators.[2]

It is noteworthy, however, that eosinophils, the presence of which many workers have emphasized, were relatively rare in the sections from our case and that there was no increase of these cells in the blood. Plasma cells, on the contrary, constituted a prominent feature of the cellular reaction.

The widespread lesions in the respiratory tract, pharynx, larynx, trachea and bronchi, we have interpreted as a part of the pemphigus. While there is clearly present an acute bacterial infection—as evidenced by gram-positive cocci in the mucosa—and an acute inflammatory reaction, this is obviously superimposed on a subacute or chronic inflammatory process. The microscopic changes in the submucosa of the trachea and bronchi simulate closely those in the skin and leave little doubt as to their relationship. Pemphigus of the respiratory tract, generally but not always associated with cutaneous lesions, has been described by several investigators,[3] but in most cases the changes have not been carefully studied histologically.

While there may have been no previous attempt to separate such cases as Brocq describes into a distinct group, it is probable that most dermatologists of large experience have encountered cases which did not conform to the usual type of chronic pemphigus and which may properly be placed in this group. In this country such cases have usually been grouped under pemphigus vulgaris (chronic or true pemphigus), and have frequently been designated as malignant.

A case of this type, which showed a slight tendency to vegetations in some of the lesions, was reported in 1905 by Ormsby and Bassoe,[4] who also refer to similar cases. At that time the question was raised as to whether the case should be classed as pemphigus vegetans. Later, in his textbook, Ormsby placed this case under pemphigus vulgaris, remarking:

> That certain examples of pemphigus belonging to this group are acute in nature seems to be a fact. A number of cases have been under observation during the past few years. One of these was reported conjointly by the author

2. Spiegler in Mracek: Handbuch der Hautkrankheiten **2**:23, 1905. Ehrmann und Fick: Kompendium der Speciellen Histopathologie der Haut, Wien 1906, p. 13.

3. Trautmann: Die Krankheiten der Mundhöhle und der oberen Luftwege bei Dermatosen, Wiesbaden, 1911.

4. Ormsby and Bassoe: A Case of Acute Malignant Pemphigus (P. vegetans?) with Autopsy Report, J. Cutan. Dis. **23**:294, 1905.

with Dr. Peter Bassoe. In this case the lesions originated in the mouth and the disease proved fatal in two months. Extensive cutaneous involvement occurred with the formation of bullae and severe extensive erosions of the skin. There was practically no attempt at healing in any of the denuded areas. This history could be repeated many times by patients seen during the last few years.[5]

Brocq's articles, by calling attention to this syndrome, may lead to a detailed study of a larger number of cases, which may possibly bring about a more definite conclusion in regard to these cases, though we can expect little information from the study of the histopathology and bacteriology. In one of Brocq's cases there was a growth of a mixture of staphylococci, streptococci, diplococci and bacilli, which he attributes, no doubt correctly, to a contamination from the surface of the body.

Brocq does not pretend to fix this syndrome definitely as a new clinical entity. He simply notes that the appearance and evolution of the syndrome which he sketches seems to be quite characteristic, and inquires whether this syndrome is always a primary condition or whether it may not be sometimes a syndrome which may be grafted on another bullous dermatosis, especially on a dermatitis herpetiformis, dermatite polymorphe or a chronic pemphigus. Among several cases reported, he cites one which tends to support the latter view. And in one patient, an 18 months old child, he questions whether the syndrome was not a variety of impetigo similar to pemphigus neonatorum.

Until some fruitful researches have thrown some light on the etiology and pathogenesis of pemphigus it may be idle to speculate on the place of this group of cases in the general scheme. At present, however, in their clinical characteristics they appear to us to be more closely related to chronic pemphigus and to acute febrile pemphigus.

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5. Ormsby, O. S.: Diseases of the Skin, Ed. 2, 1921, p. 375.

SYPHILIS AND TUBERCULOSIS

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The subject, which this communication embraces, is one frequently discussed, but the case reported shows such varied and interesting pathologic manifestations that it seems well worth the effort to compile detailed data on it.

REPORT OF A CASE

History.—R. S., aged 48, colored, a cook and fish peddler, living at Ford City, Pa., was referred to the dermatologic department of the Passavant Hospital of Pittsburgh, Oct. 6, 1920, on account of extensive bilateral ulcerations on his neck.

He gave the following history: About a year ago he noticed a few deep-seated lesions on his face and neck, continuously enlarging. Within four weeks most of these lesions broke down and formed ulcers, which remained in the same condition for a considerable period until the patient's physician gave him seven intravenous injections of arsphenamin; a slight improvement was noted, and the ulcers healed partially except at the nape of the neck and about the ears where they remained unaffected by the treatment and continued to discharge profusely a greenish pus, which was very offensive.

About the time of the appearance of these ulcers, the patient's legs began to swell; this edema was especially noticeable about his ankles; at first it would subside during the night, but during the last three months it became rather stationary, being aggravated only if he was more active than usual. Concurrently with this edema, he noticed, a gradually beginning dyspnea, exaggerated on climbing stairs, with occasional pain in the precordium. All of these symptoms improved after antisyphilitic treatment.

He had been very miserable since the edema became generalized; the greatest inconvenience was caused by the edema about the testicles and penis, interfering with urination. His appetite was good. Bowel movement was interfered with by hemorrhoids, which bled frequently and freely. He tired quickly, slept well and had no headaches.

He had had a chancre ten years ago which had been untreated. Gonorrhea was his "constant companion" as he put it. Outside of these two diseases he had never been ill.

He had been married for twenty-three years; his wife had had four miscarriages, but had no living children. He used tobacco and coffee to excess, and he drank alcoholic beverages in moderation. His father died of cardiac disease. His mother died of tuberculosis. He had five brothers who were well; one brother had died of tuberculosis. One aunt had scrofula.

Physical Examination.—The patient was lying in bed propped on several pillows; his breathing was heavy and labored. Although his entire body was edematous, his face was strangely narrow and thin, and his cheek bones were very prominent. He answered questions very intelligently. He did not look older than his age. The skin all over his body was puffed and there was

marked indentation on pressure; however, it felt very dry and especially over the abdomen it was scaling; the condition had the appearance of ichthyosis simplex. There were three large ulcerative areas on the lateral surface of the neck—one on the right side extending from the clavicle 6 cm. upward and 16 cm. transversely, and two ulcerating surfaces almost sym-

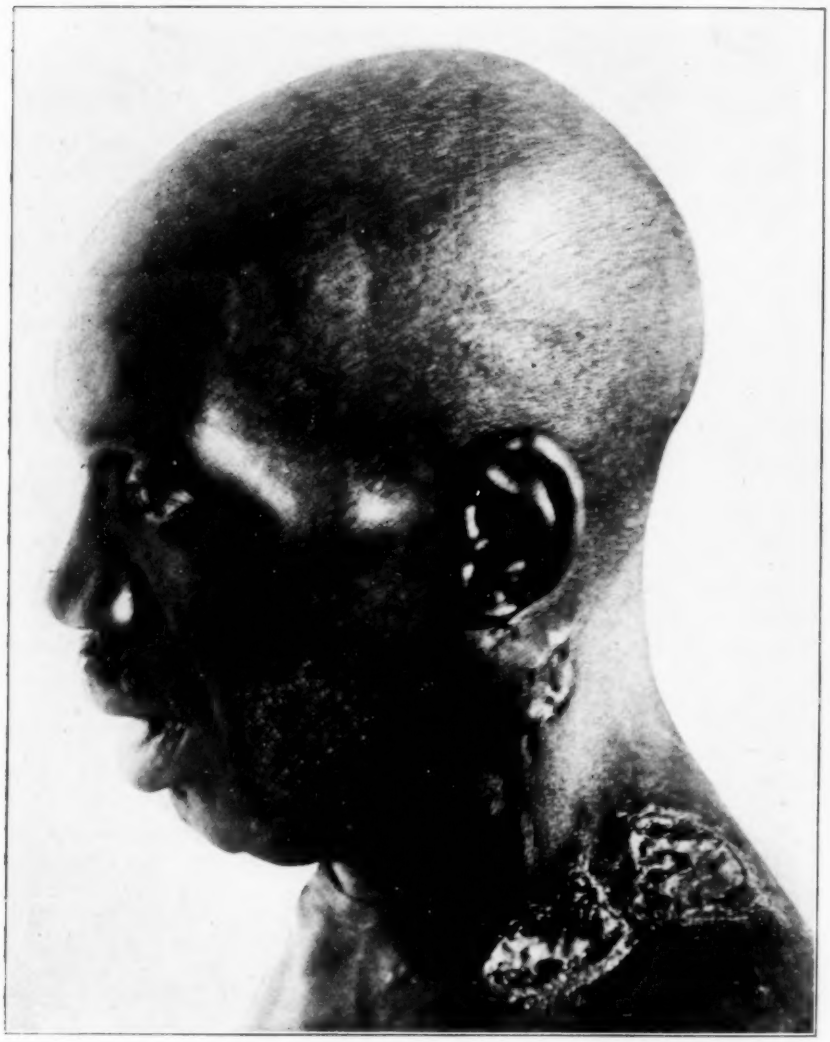

Fig. 1.—Two ulcers on the left side of the neck.

metrically placed to the one on the right side were found on the opposite lateral surface.

The borders of all were irregular, circinate in the large one, kidney shaped in the other two, with deeply punched out uneven edges, definitely undermined; all were partially covered by brownish green crusts, which were easily elevated

and left an uneven reddish-gray base, protruding in areas, depressed elsewhere. There was a profuse discharge, which seemed to pour out of the ulcers, bathing the base.

On either side leading from these areas of ulceration there was a fan-shaped scar which extended to the ear and showed keloid formation in areas. It looked like a healthy scar, the pigmentation of which was much lighter than the surrounding skin.

The eyes reacted to light and accommodation; the elbow and knee reflexes appeared to be normal. The Romberg sign was slightly positive. The gait could not be observed well, as walking caused dyspnea at this time. At a later date his gait was normal.

Laboratory Findings.—The roentgen-ray examination revealed enlarged mediastinal glands, which were probably syphilitic.

Fig. 2—Tuberculosis peritonitis.

Blood examination revealed: red blood cells, 5,100,000; white blood cells, 13,200. The result of the differential count was: polymorphonuclears, 54 per cent.; small mononuclears, 38 per cent., and large mononuclears, 8 per cent. Blood Wassermann reaction: cholestrinized antigen, ++++; acetone insoluble lipoids, ++++. The icebox method of fixation yielded the same result.

Urine: Albumin was present. There were a large number of casts.

Diagnosis.—The diagnosis was tertiary syphilis; tuberculonodular ulcerative gummas.

History of Disease and Treatment.—On account of the generalized anasarca, the patient was put on an elimination treatment, sodium citrate, 15 grains, three times a day.

His fluid intake was restricted and one ounce of castor oil was ordered every second day, with absolute rest in bed. In ten days his general condition improved remarkably, and he was put on potassium iodid, 30 grains daily, and increased 3 grains every day.

On the fourteenth day, 0.4 gm. of neo-arsphenamin was given intravenously and again on the eighteenth day. Within twenty-four hours after the second dose of neo-arsphenamin the patient was again water-logged, and albumin was present in his urine. We then decided to discontinue the neo-arsphenamin treatment, and continued administering potassium iodid in increasing doses until the forty-third day. The ulcers had healed and the edema had disappeared; the patient felt well enough to go to his home. He was put on small doses of mercury (Hydrargyri chloridum corrosivum 1-16 gm., three times a day and instructed to return to our dispensary once a week. On these visits, after an examination of the urine the patient was given mercury salicylate, 1 grain, intramuscularly. He continued to improve and gain weight and went to work on a wagon the second week in December.

Fig. 3.—Multiple gumma of the liver.

On Jan. 1, 1921, the patient suddenly developed ascites, began to feel dizzy and weak, and was readmitted to the hospital on Jan. 2, 1921.

Three liters of turbid fluid were recovered by paracentesis, after which the patient seemed to improve greatly. Our laboratory reported that the fluid formed a "web" on standing. The smear showed a large number of cells, 95 per cent. of which were small lymphocytes, 4 per cent. endothelial cells and 1 per cent. polymorphonuclears. Wassermann reaction: cholestrinized antigen, ++++; acetone insoluble lipoids, ++++. The icebox method yielded the same result. Microscopic examination for tubercle bacillus was negative.

One hundred c.c. of the fluid from the abdomen were centrifuged at high speed for twenty minutes, and the sediment diluted with 2 c.c. of sterile salt

solution. The fluid was injected subcutaneously into the upper left thigh of a guinea-pig after trauma of the lymph nodes in the left groin. Feb. 24, 1921, the pig was alive and well; there was no adenopathy.

A weak and slightly irregular pulse, ranging from 86 to 106, and temperature mostly subnormal, usually about 97 F., but on one occasion rising to 100 F., completed the picture, which the patient presented. He was languid, but showed no sign of acute illness or of oncoming death.

With the report of an exudate, instead of a transudate, which was expected, the diagnosis of hepatic cirrhosis was eliminated, tuberculous peritonitis, which

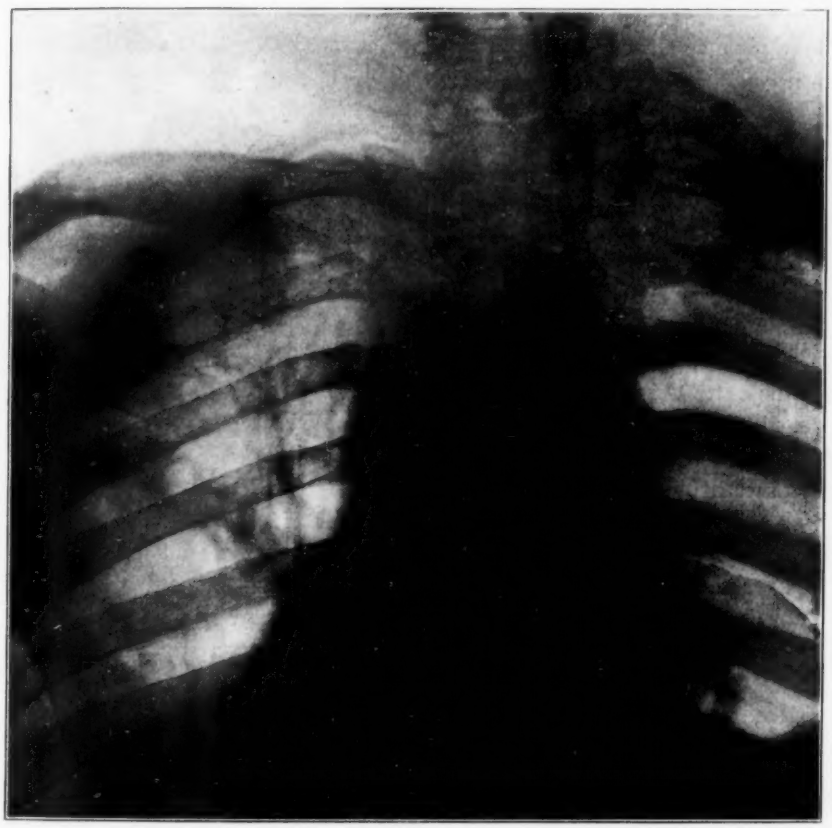

Fig. 4.—Mediastinal adenopathy before treatment.

was greatly anticipated, was only tentatively made on account of the lack of tenderness in the abdomen.

Within forty-eight hours the patient was so distended again that a second paracentesis was performed, and 2 liters of the same type of fluid was recovered as before.

A further search in order to clear up the diagnosis was made by requesting a comparative roentgen-ray study of the size of the mediastinal glands which on October 7 were definitely hypertrophied. These gland shadows had disappeared

almost entirely or practically so, according to the roentgen-ray findings, and we felt reasonably certain that these glands, which we thought syphilitic, had disappeared under the influence of antisyphilitic treatment.

The further course of this patient was unsatisfactory. He was steadily loosing ground until January 12 when the patient became delirious and expired at 1:45 a. m.

Necropsy Findings.—The findings were: tuberculous peritonitis, ulcerative tuberculous enteritis, tuberculous mediastinal and mesenteric adenitis, ulcerative tuberculous pneumonitis (left), ulcerative tuberculous bronchitis, healed tuberculosis of the right lung, chronic fibrous pleuritis (right), chronic interstitial nephritis with parenchymatous degeneration, amyloid infiltration of kidneys, acute localized nephritis (right), amyloid and fatty infiltration of the liver, multiple gummas of the liver with hepar lobatum, gummatous adenitis of the saphenous glands, syphilitic aortitis, slight mitral stenosis.[1]

DISCUSSION

There are several points of distinct interest in this case—gumma of the lymph nodes are uncommon enough to merit special mention. We always consider syphilitic scars as healthy ones, in differentiation from tuberculous scars, and usually after a destructive syphilitic process the resultant scar remains healthy. In the present case the ulcerations on the patient's neck occurred within a scar, which gave all the appearance of a healed syphilitic ulcer and with which the history of the patient was consistent. At the beginning of the skin manifestations, that is one year before the patient's death, these ulcerations began and under antisyphilitic treatment became absorbed. This happened during the first sojourn of the patient in the hospital, when these ulcerations healed well and quickly under mild antispecific treatment. The bilateral character of a tertiary syphilitic manifestation of the same character is also not frequent enough so that a notation should not be necessary.

We believe that the mediastinal adenitis revealed by the roentgen-ray examination, which was attributed at that time to a syphilitic process and its later disappearance to antisyphilitic treatment, should be considered in a different light. At necropsy these glands were found to be caseating and gave a typical picture of tuberculosis. At the time of the first roentgen-ray examination they were probably edematous, entering into the general picture of anasarca; later their size lessened, when this vascular syndrome was brought under control.

The question of medication is worthy of discussion. Here we had a patient in need of active treatment, whose kidney function was so interfered with that both mercury and arsenic could be administered only cautiously or not at all. Two doses of neo-arsphenamin produced a generalized anasarca so that we had to discontinue this type of therapy.

1. We find it necessary to confine ourselves to the mere enumeration of pathologic findings on account of brevity. A detailed report of the necropsy findings will be furnished on request.

Urine showing the presence of continued albumin kept us at bay with mercury at the institution of his treatment. Iodids were the only therapeutic measure left. Clinical experience teaches the inadvisability of administration of iodids in tuberculous patients, and the only reason we can give for their administration was that at the institution in which this patient was treated we could see no contraindication. His fairly normal temperature and lack of other symptoms or physical signs put us off our guard. The very fact that the patient continued to improve under the effect of iodids, by the recession of anasarca, dyspnea, healing of ulcers, and the feeling of well being, the gain in strength (physical) and weight did not show that the iodids might defeat our purpose.

His sudden collapse, after about four weeks of well being, and the marked nature of his miliary tuberculosis, on the other hand, seem to indicate that the body which was able to withstand the assaults of this double infection in a fairly efficient manner for years lost resisting ability all at once as it seemed and permitted an unchecked spread of tuberculosis in an uncontrollable manner. How much of this was caused or facilitated by the administration of iodids, as much as 90 grains a day being given, can only be assumed.

Literature is swarming with observations and statistics of the frequency with which these two diseases exist concurrently in the same person.

Ravogli [2] says in many cases tuberculosis is also associated with syphilis, and together they cause the most hideous ulcers and extensive destructions, especially at the vulva.

He [3] also states that tuberculosis has a great influence on the course and malignancy of syphilis. It seems that the tubercle bacillus, in consequence of the new syphilitic infection, takes on an extraordinary activity, and in this way syphilis assumes malignant forms. Tuberculosis which was latent during good health, in consequence of the syphilitic infection shows itself with quick and destructive results. It is incredible that the two infections have such a direct influence on one another that when syphilis runs a severe course tuberculosis usually supervenes and ends the life of the patient.

Ravogli [4] also quotes Hochsinger, who found in children with hereditary syphilis a favorable ground for the reception and development of tuberculosis.

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2. Ravogli, A.: Syphilis in Its Medical, Medicolegal and Sociological Aspects, New York, The Grafton Press, 1907, p. 58.

3. Ravogli, A.: Syphilis in Its Medical, Medicolegal and Sociological Aspects, p. 140.

4. Ravogli, A.: Syphilis in Its Medical, Medicolegal and Sociological Aspects, p. 165.

Morris [5] asserts that syphilis predisposes to tuberculosis.

Vedder [6] says that "Syphilis makes the bed for tuberculosis." He quotes Brock who, after investigating 7,660 consecutive South African natives among whom tuberculosis was practically unknown at that time, comes to the following conclusions:

1. Thirty-five per cent. of natives have a fibroid condition of the lungs.

2. Sixty-eight per cent. have indurated enlargement of the epitrochlear gland.

3. Both conditions result from syphilis, and nearly 80 per cent. of the natives have one or both conditions.

4. Syphilis prepares the way for tuberculosis and is in all probability the chief cause for the great prevalence of, and the high mortality from, the latter disease in the natives engaged in mine work on the Rand.

5. Syphilis plays a rôle in the production of lung diseases in the youth and adult, the great importance of which has not been recognized.

In accordance with such considerations, it would be expected that syphilis would be more prevalent among the tuberculous than among those suffering from other diseases.

Letulle, Bergeson and Lepine,[6] who for more than a year performed Wassermann tests on all patients with tuberculosis, obtained positive reactions in 19 per cent.

Marino and Fournier [7] emphasize the unsuspected frequency of inherited syphilis as a predisposing factor in status lymphaticus, asthenia and obscure endocrine derangements. Tuberculosis so often develops on a basis of syphilis that inherited syphilis should be suspected in masked cases.

In analyzing these reports of cases of tuberculous patients in whom the blood Wassermann test was performed, we have placed them in two columns: (1) those who gave unmistakable evidence of syphilis by a strong blood Wassermann reaction; these were placed in the column of "Positively Syphilitic"; (2) those who gave a lesser blood Wassermann reaction; these were placed in the "Probably Syphilitic" column.

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5. Morris, Sir Malcolm: The Nation's Health, New York, Funk and Wagnalls Co., p. 28.

6 Vedder, Edward B.: Syphilis and Public Health, Philadelphia, Lea and Febiger, 1918, p. 68.

7. Marino, E., and Mussio-Fournier, M. J. C.: Syphilis and Tuberculosis, Bull. et mém. Soc. méd. d. hôp. **43**:1002 (Nov. 28) 1919; abstr., J. A. M. A. **74**:359 (Jan. 31) 1920; also in Rev. méd. del Uruguay **22**:807, (Nov.) 1919; also in Semana méd. **27**:170 (Jan. 29) 1920; abstr., J. A. M. A. **75**:138 (July 10) 1920.

Percentage is also figured accordingly. Of the 6,324 cases examined, 494 were found definitely syphilitic, excluding 251 cases of Jones and 376 cases of Petroff. On account of lack of differentiation of strength of the blood Wassermann reaction, we find that the average of all investigators studied is 10.36 per cent. Combining the probable and positive cases, we find that of the 6,324 cases, 830 gave a positive blood Wassermann reaction of any strength; this would raise our figures to 17.81 per cent. in the total of all the cases investigated by the authors mentioned in the foregoing.

The frequency of this coexistence of diseases is well known to pathologists, who usually find many pathologic conditions in patients after death, who were not suspected of such multiplicity of lesions. This is by no means unobserved by clinicians, but we feel that it is not emphasized frequently enough.

The following table was compiled to obtain a fair average of the reports of coincidence of these two diseases.

COINCIDENCE OF TUBERCULOSIS AND SYPHILIS

Investigator	Number of Patients	Number Positively Syphilitic	Number Probably Syphilitic	Both	Positive Percentage	Total Percentage
Lettule, Bergeron and Lepine *	346	64	...	64	19.0	19.0
Vedder *	211	36	17	53	17.0	23.2
Snow and Cooper *	290	44	14	58	14.8	20.0
Lyons *	471	29	12	41	6.2	9.2
Jones *						
Dispensary	251	...	73	73	....	29.0
Hospital	189	18	...	18	11.0	25.0
Petroff *	376	...	82	82	....	21.8
Ford *	328	6	22	28	2.0	8.0
Collectanea,* N. Y. Med. J.	175	14	9	23	8.0	13.1
H. J. Cooper *	2,794	181	...	181	6.5	6.5
Day, A. B. and McNutt, W. †	893	102	107	209	11.3	23.4
	6,324	494	...	830	10.36	17.81

* Vedder, Edward B.: Syphilis and Public Health, Philadelphia, Lea and Febiger, 1918, pp. 68, 69, 70 and 107.

† Day, A. B., and McNutt, W.: The Incidence of Syphilis as Manifested by Routine Wassermann Reaction in Two Thousand Nine Hundred and Twenty-Five Hospital and Dispensary Medical Cases, Trans. Assn. Am. Physicians, **34**: 345-352, 1919.

CONCLUSIONS

1. A case has been presented in which the patient showed gross syphilitic and tuberculous lesions.

2. Available statistics of the coexistence of syphilis and tuberculosis have been reviewed.

3. The possible malignancy of tuberculosis in the case described is attributed in part at least to iodid medication.

We wish to express our thanks to George W. Grier, M.D., for the roentgen-ray study of this case.

SYNOVIAL LESIONS OF THE SKIN

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AND
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Attention was first called to synovial lesions of the skin by Hyde [1] in 1883. More recently the subject has been discussed by Lingenfelter,[2] Ormsby,[3] and Sutton.[4]

Synovial lesions of the skin occur over the dorsal aspects of the interphalangeal, metacarpo-phalangeal and metatarso-phalangeal articulations. The most frequent situation is over the dorsum of the articulation between the distal and adjacent phalanges of the index finger and thumb.

There is usually a history, extending at least over several months, of the appearance in one of these situations of a small, globular projection from the skin, which is insensitive unless roughly handled, and which slowly develops to the size of a large pea. When punctured a syrupy, whitish, yellowish or brownish, fluid exudes, occasionally mingled with masses like sago grains. As the lesion develops, it ordinarily assumes the appearance of a vesicle or bulla; some lesions have only an epidermic roof-wall and are exceedingly painful, especially when on the feet. The surface of the lesion is generally smooth and shiny and shows more or less telangiectasia. It may appear roughened or moderately verrucous. It may therefore be slightly warty in appearance, but it is more likely to suggest a thick-walled cyst. The lesion is usually translucent or semitranslucent. Fluctuation is usually present, but there are no signs of infection. Bacteriologic examinations of the fluid have yielded negative results in the cases cited by Drs. Ormsby and Lingenfelter. Immediately subsequent to puncture the cyst collapses, but after the lapse of a week or more the cavity refills with a similar gelatinous, glairy fluid.

The pathogenesis is problematical. Anatomically there are no well-defined bursae in these situations; the lesions that have been radiographed show apparent relationship to the underlying articulations.

Ganglions of the fingers most frequently occur on the flexor aspects, and often show similar connections with the adjacent joint cavities.

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1. Hyde: Diseases of the Skin, Ed. 1, Philadelphia, 1883, p. 444.
2. Lingenfelter: Jour. Cutan. Dis. **31**:647, 1913.
3. Ormsby: Jour. Cutan. Dis. **31**:943, 1913.
4. Sutton: Diseases of the Skin, Ed. 3, St. Louis, The C. V. Mosby Co., 1919, p. 436.

Fig. 1 (Case 1).—Lesion on middle finger of the right hand.

Fig. 2 (Case 1).—Roentgenogram of lesion.

They have been regarded by many as herniae of the synovial membrane of a joint or tendon sheath through its capsule or fibrous sheath, described by Jordan as "a sudden extrusion of the synovial membrane through a chink in the capsule of a joint or tendon sheath." Later a plastic inflammation closes the outlet. Other observers believe that certain folds and crypts, occurring in synovial membrane lining joints and tendon sheaths, are of such a character that pockets of unobliterated synovial membrane may be occluded by inflammatory adhesions in the outlets of the crypts or folds leading to the synovial cavity. As the synovial membrane continues to secrete, a cyst is formed away from the joint or tendon sheath.

Adventitious bursae frequently occur in areas in which anatomic or regularly described bursae are never found, particularly over bony prominences subjected to pressure or friction for long periods of time. Clarke [5] states that "the development of an adventitious bursa takes place through a physiological metamorphosis in the connective tissue cells to meet the requirements of the body, similar to the development of an anatomical bursa," and he does not believe that they are formed by cystic degeneration of connective tissue as ganglions frequently are. Fetal sequestration has also been mentioned as a cause of ganglions, as in dermoid cysts. Clarke is "positive that many ganglia are distended anatomical or adventitious bursae, but the majority are connective tissue cysts, formed by degeneration excited by unknown factors. Ganglia are very rarely hernial protrusions."

Most synovial lesions of the skin originate from, or are distended, hydropic adventitious or anatomic, bursae. Some of them seem to show, roentgenographically, connections with the joints. If these connections have been patulous, they have been closed because pressure on the cysts does not show any patent connection with the articular cavity. In their articular relations the synovial lesions of the skin suggest a relationship to ganglions.

AUTHORS' CASES

The condition is rare, or at least uncommon. We have seen two cases. The first was of twenty years' duration. The lesion occurred in a man 26 years of age, and was situated over the dorsal aspect of the distal interphalangeal articulation of the middle finger of the right hand. It consisted of a pea-sized, smooth, shiny, transluscent, rounded, cystic tumor with a thick wall; it was not painful; there were a few visible venules in its wall. On palpation the tumor was firm but not hard. There was a sense of fluctuation.

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5. Clarke: The Pathogenesis of Ganglia, Surg., Gynec. & Obst., July, 1908, p. 56.

Fig. 3 (Case 2).—Patient's right hand before and after treatment.

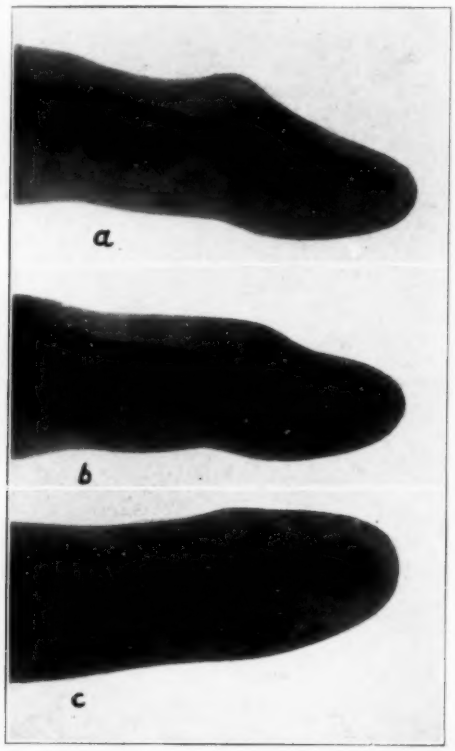

Fig. 4.—*a*, roentgenogram of portion of right index finger before treatment, *b* and *c*, side and front view after treatment.

Fig. 5.—Lesion on right middle finger (Dr. Pusey's case).

The second case was of five months' duration, and occurred in a woman 48 years of age. The lesion was situated over the dorsal surface of the distal interphalangeal joint of the right index finger. It was painless, globular, tense, semitranslucent, pearly in color, and the size of a large pea. Pressure caused a hyperemic areola at its circumference and a pallor of its central portion. This was probably caused by the occlusion of the small vessels in the walls of the lesion. The walls were thick, tough, smooth, shiny and slightly telangiectatic. Fluctuation was present.

Roentgenograms of each of these cases, as in the case described by Lingenfelter, showed no bone involvement; but the roentgenograms in both our cases showed plainly a connection with the joint cavity.

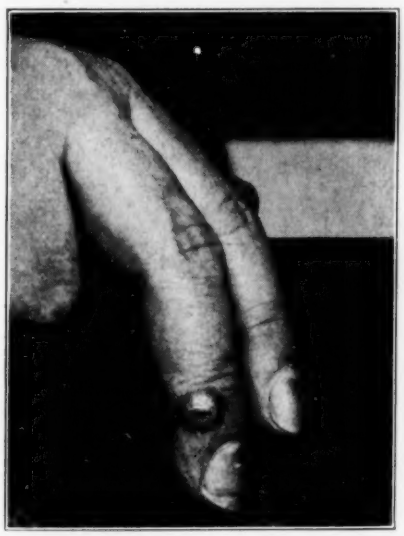

Fig. 6.—Lesion on right middle finger (Dr. Pusey's case).

DR. PUSEY'S CASES

Through the kindness of Dr. William Allen Pusey, we include herewith a description of two cases of synovial lesions of the skin occurring in man and wife. This peculiar coincidence is itself worth recording. Clinically the lesions resembled our two cases. We are fortunate in being able to present photographs of each case (Fig. 5, husband, and Fig. 6, wife). The histopathology of Figure 6 as recorded by Dr. Pusey follows:

The sections show a sharply circumscribed fibrous tissue growth, the central part of which appears to have undergone myxomatous degeneration. In this myxomatous tissue there are several cysts, the walls of which are formed by compression of the surrounding myxomatous tissue. These cysts have no

endothelial or epithelial lining, nor do they or the tumor itself show any connection with a deeper structure. The whole tumor has compressed the surrounding tissue more or less; especially is this well marked in the lower part of the section where coil glands are found in this compressed wall.

TREATMENT

The treatment requires the complete destruction or excision of the entire secreting cyst wall. Lesions have been carefully dissected out, but the removal must be complete or recurrence takes place. Our first patient was so treated, and there was no recurrence. Roentgenotherapy is the method of choice. Hyde and Ormsby employed unfiltered roentgen rays successfully in several cases; the technic was fractional (several small doses). Sutton used radium with satisfactory results in one case (40 milligram hours, unscreened).

The lesions in our second case disappeared completely after one roentgen-ray exposure. The technic was: A dose of 1 Holzknecht unit skin distance (one skin unit) unfiltered was applied to each side of the tumor. The articulation was included in the field of radiation. Four weeks after this "cross-fire" treatment the lesion had completely disappeared, and a second exposure of 1 Holzknecht unit skin distance, unfiltered, was given to its previous site. A roentgenogram two weeks later showed that the subcutaneous portion, which was connected with the joint, had entirely disappeared.

Refrigeration (carbon-dioxid snow) and electrolysis have been used.[6]

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6. In addition to the references given, the following may be of interest:
Jones and Meakins: Cited by Hyde.
Jordan: Ganglion, Lancet **2**:242, 1893.

STOMATITIS AND APLASTIC ANEMIA DUE TO NEO-ARSPHENAMIN *

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Among the late reactions occurring after the use of arsphenamin products in the treatment of syphilis, the most serious are dermatitis, stomatitis, jaundice and encephalitis. In this country the last is rarely encountered, although it is apparently quite frequent in Europe. The other reactions mentioned are more common and are thus of greater practical importance. Dermatitis and stomatitis appear to be closely allied. Previous papers [1] from this clinic have discussed this interrelation, and have drawn attention to a characteristic common to both types of reaction, namely, a striking alteration in the blood picture during life and marked changes in the bone marrow at necropsy.

Since any data which may tend to throw light on the mechanism of these reactions should be presented, the following case report is believed to be worthy of record.

REPORT OF A CASE

History.—A white woman, aged 50, had been twice married. The first husband had died some years ago, cause unknown. The issue from this marriage was one daughter, well at the age of 28, with no stigmas of congenital syphilis, who herself has several normal children. During the first marriage there were no miscarriages and no history of possible signs of syphilis.

In 1918, the patient married again, a marriage of convenience, with a man twelve years her senior. Owing to the character of the marriage there was no sexual intercourse until February, 1919, and this took place only once. Intromission was not effected, but ejaculation took place, and semen was deposited on the vulva. At the time the patient had an open abrasion on the inner surface of one labium majus. A few weeks later, after the abrasion had healed, there appeared in its exact location a small painless erosion. This was followed in a few weeks by general malaise and headache. In May, 1919, she was seen by one of us.

Physical Status.—The patient was obese, but was otherwise in excellent physical condition. Examination of the central nervous system and of the cardiovascular system were negative. On the inner surface of the left labium majus near the fourchet was a small oval erosion about 0.75 by 1.0 cm.,

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* From the Syphilis Department of the Medical Clinic, Johns Hopkins Hospital.

1. Moore, J. E., and Foley, F. E. B.: Serious Reactions from the Salvarsan and Diarsenol Brands of Arsphenamin: Unusual Blood Pictures with the Report of a Fatal Case, Arch. Dermat. & Syph. **1**:25 (Jan.) 1920. Moore, J. E., and Keidel, A.: Dermatitis and Allied Reactions Following the Arsenical Treatment of Syphilis, to appear in Arch. Int. Med.

slightly elevated, dusky red, indurated and painless. There was slight painless discrete left inguinal adenopathy. Careful examination of the skin, mucous membranes and glands failed to disclose any secondary manifestations. Dark-field examination of the secretion from the labial lesion showed many actively motile *Spirochaetae pallidae*. The blood Wassermann reaction was positive.

The husband denied any definite history of syphilis but admitted several genital sores early in life. Examination revealed aniscoria, sluggish irregular pupils, and sluggish knee and ankle jerks, more active on the left. The gonads were normal to palpation. The blood Wassermann reaction was positive, but spinal puncture was refused. However, evidence corroborating the clinical diagnosis of neurosyphilis was obtained by the fact that this patient was Wassermann-fast. Twenty-four doses of arsphenamin with interim mercury by inunction failed to reverse the positive blood Wassermann reaction.

TABLE 1.—Treatment Administered

Date, 1919	Drug	Blood Wassermann Reaction	Remarks
May 17	Arsphenamin 0.4 gm.	Positive	Slight erythematous rash, appearing 24 hours after treatment, lasting 36 hours
May 21	Arsphenamin 0.3 gm.	Positive	Recurrence of skin rash, maculopapular rash, of greater intensity, lasting 4 days, and accompanied by much itching
May-Nov. inclusive	Mercurial ointment 33%		
July 2	.....	Negative	
Sept. 3	.....	Negative	
Dec. 6	Neo-arsphenamin 0.3 gm.	Negative	No generalized skin rash. Two days later profuse crop of herpes, upper lip; also coryza, which may have caused herpes. About 5 hours after the injection, chill, nausea and headache, and for the next 3 to 4 days generally knocked out
1920			
Jan. 6	Neo-arsphenamin 0.3 gm.	Anticomplementary	After this and each succeeding treatment, marked malaise lasting several days
Jan. 16	Neo-arsphenamin 0.3 gm.		
Jan. 26	Neo-arsphenamin 0.45 gm.	Anticomplementary	
Jan. 30-Feb. 10	.....	.....	Influenza
Feb. 26	.....	Negative	
Feb. 25-April 15	Mercurial ointment 33%		
April 19	Neo-arsphenamin 0.3 gm.	Negative	
April 28	Neo-arsphenamin 0.3 gm.	Negative	
May 10	Neo-arsphenamin 0.3 gm.	Negative	
May 15	Neo-arsphenamin 0.3 gm.	Negative	
May 25	Neo-arsphenamin 0.3 gm.	Negative	See text

Diagnosis: Primary syphilis, contracted by seminal injection.

Treatment and Course.—Treatment was begun on the day of the first visit and was continued as shown in Table 1.

After the last treatment, on May 25, the patient left Baltimore for the seashore, where she remained a week. On the train, about six hours after the treatment, she suffered with chilly sensations and vertigo. Within a day or so after her arrival at the shore, she felt miserable and for the next week had some fever, her mouth became sore, and she gradually became jaundiced. On June 2, she returned to Baltimore, and was seen late that evening at her hotel.

Her temperature was 101 F., pulse 110. The skin and sclerae were slightly jaundiced. The gums were tender, swollen and bleeding, and the teeth were loose. Around the first upper left molar was a purplish discoloration, and on the hard palate was a huge ecchymosis. Small purpuric spots covered the hands and arms, and there was a large ecchymosis of the left shoulder. During the next two weeks she grew steadily worse and gradually became profoundly ill. Her temperature remained constantly elevated, ranging from 101 to 105 F. Fresh hemorrhages, petechial and ecchymotic, constantly appeared in the skin and mucous membranes, and there was intermittently severe epistaxis, bleeding from the gums and vagina. Blood was found in the urine and stools. The condition of the mouth grew much worse. The gums became purplish red, covered with a thick purulent discharge; the teeth were loose; a large

TABLE 2.—STUDIES OF THE BLOOD

Date	Red Blood Cells	Hemoglobin, per Cent.	White Blood Cells	Differential, per Cent.						Platelets	Remarks	Medication
				P. M. N.	P. M. B.	P. M. E.	S. M.	L. M.-T.	Myob.			
May 25	.....	..	....	...	..	...	...	...	...	.....	.....	Neo-arsphenamin 0.3 gm.
June 4	3,176,000	64	1,100	11.0	—	5.0	76.0	8.0	—	None seen		
June 5	3,832,000	75	1,600	17.0	—	1.0	79.0	3.0	—	None seen		
June 6	.....	..	....	...	..	...	...	...	...	.....	.....	Transfusion 1
June 7	4,128,000	81	1,000	15.0	—	—	78.0	7.0	—	None seen		
June 9	4,192,000	79	800	...	..	...	...	...	...	.....	Coagulation time (Boggs) 6 min.	Transfusion 2
June 10	3,856,000	76	600	10.6	—	1.3	81.4	5.4	1.3			
June 12	4,112,000	74	800	9.0	—	—	89.0	2.0	—	48,000		
June 14	3,456,000	78	950	12.0	—	2.0	83.0	3.0	—			
June 16	3,616,000	83	950	5.0	—	2.0	91.0	2.0	—	.....	Coagulation time 7 minutes	Transfusion 3
June 17	4,000,000	..	....	...	..	...	...	...	...	48,000	Vital staining reticulated cells 0.4 per cent.	
June 18	3,872,000	81	550	4.0	..	—	94.0	2.0	—	28,000	Reticulated cells 0	
June 19	3,920,000	..	....	...	..	...	...	...	...	36,800	Reticulated cells 0	Transfusion 4
June 20	2,992,000	76	900	6.0	—	—	92.0	2.0	—			
June 21	3,000,000	..	....	...	..	...	...	...	...	28,800		
June 22	.....	..	....	...	..	...	...	...	...	.....	Died	

necrotic ulcer appeared in the hard palate. Two small pinhead-sized ulcers appeared on the skin, at the angle of the mouth and on one ala nasi, and rapidly increased in size until each was as large as a dime. The base of each was black, composed of necrotic tissue resembling an eschar. Drowsiness was a constant and marked feature, and toward the end the patient complained bitterly of headache. Examination of the heart, lungs and abdomen was always negative.

Treatment was symptomatic only. On June 6, 9, 16 and 19 transfusions of 250 c.c. each of matched citrated blood (Group 4) were administered, without reaction or beneficial effect. The patient gradually grew weaker and died on June 22, four weeks after the onset of the reaction.

Laboratory Data.—Smear from the exudate about the teeth showed many spirochetes and fusiform bacilli, a typical picture of Vincent's angina.

Urine: Specific gravity was low and fixed (1.002 to 1.010). There was a constant trace of albumin, and after June 10 numerous red blood cells and a strongly positive benzidin test. Phthalein (June 9) was 55 per cent. in two hours.

Stool: June 11, there were no blood (benzidin), ova or parasites. June 18, there was bloody mucus, benzidin positive. Thereafter blood was constant.

Blood Culture: June 8, the culture was negative. June 19, Friedländer's bacillus (agonal invader?) was found.

Blood Chemistry: June 12, calcium, 9.7 mg. per 100 c.c. (normal limits), was found.

Blood: See Table 2.

Necropsy Examination (Dr. Webster).—This was performed ninety minutes after death.

Anatomic Diagnosis: The diagnosis was: extensive subcutaneous and subserous hemorrhages; submucous hemorrhages of stomach, intestines and liver; hemorrhagic nephritis; aplastic bone marrow; lobular pneumonia; edema of lungs; arteriosclerosis.

Body: Numerous large and small petechiae were seen in the skin over the posterior surface of the arms and over the chest and abdomen. The skin of the face and neck was lemon yellow, and over the chest and abdomen, subicteric. The subcutaneous tissues were not edematous. The sclerae and conjunctivae were distinctly yellow. The external nares were occluded by recent hemorrhagic clots and were surrounded by scaly excoriations. There was an ulcer about 1 cm. in diameter on the left side of the nose. Its skin edges were purplish, its base formed by granulation tissue. The entire left side of the nose appeared purplish. A similar ulcer appeared on the mucocutaneous border of the mouth at the right side. The mucous membranes of the mouth were roughened and ulcerated and covered with a purulent material which was also oozing from the region of the gums. On the sides of the neck were a number of small indurated purplish areas.

On opening the peritoneal cavity the serous surfaces appeared smooth and transparent. No free fluid was seen. The small intestines appeared dark, and the transverse colon showed a number of hemorrhages beneath the serosa. The liver and spleen did not extend below the costal margin. On opening the chest cavities no free fluid was seen. The pleural surfaces were delicate and transparent and showed extensive hemorrhages both in the visceral and the parietal layers.

Heart: The heart weighed 325 gm. Its epicardial surface was smooth and glistening, showing large and small ecchymoses toward the base. On section the endocardium was also transparent and normal in appearance, although it covered a number of large and small hemorrhages. The cardiac chambers were not dilated or hypertrophied. The valve leaflets were normal. At the base of the aortic and mitral valves a number of atheromatous patches were seen. The coronary arteries also showed signs of arteriosclerosis. The base of the aorta, however, was elastic and lined with a smooth intima.

Aorta: The aorta had lost its elasticity. On section it presented a remarkable picture of advanced and extensive arteriosclerosis. Waxy patches were seen about the orifices of the smaller vessels. Atheromatous ulcers, fresh and hemorrhagic, were seen throughout its length. One in particular, near the bifurcation, had ruptured through the intima and media, leaving only the thin adventitia.

Lungs: The lungs were deeply pigmented and heavy. Beneath the pleura, particularly of the lower lobes, petechiae and ecchymoses were numerous. On

palpation several irregular nodules were felt in the lower lobes. On section the lower lobes were found to be congested and showed a few irregularly outlined areas of consolidation about the smaller bronchi. Both lungs were soggy and exuded a large amount of fluid, and the alveoli contained a gelatinous semifluid substance. The bronchi were slightly injected.

Spleen: Its capsule was wrinkled and slightly roughened. On section the cut surface was found to be deep red and firm. The trabeculae and blood vessels and malpighian bodies stood out sharply.

Liver: The liver weighed 1,800 gm. and measured 20 by 22 by 10 cm. Its capsule was delicate and transparent. On section the cut surface appeared pale and firm and showed the usual architecture. The lobules stood out distinctly. There was no increase in connective tissue and no areas of necrosis were present. Scattered about were a number of indefinitely outlined hemorrhages.

Suprarenals: The suprarenals weighed 15 gm. each and were normal externally and on section.

Kidneys: The kidneys weighed 120 gm. each and measured 11 by 6 by 3 cm. The capsule stripped easily, showing a number of small petechiae scattered over the surface. On section the cortex measured about 1.5 cm. in thickness. The striae were parallel and regular. The glomeruli were distinct. Here, also, small hemorrhages were observed. Deep in the pyramids were several large extravasations of fresh blood. The blood in the larger veins had clotted and distended the lumina. The pelves, however, were smoothly lined and appeared normal. The ureters also showed nothing unusual.

Gastro-Intestinal Tract: The esophagus was normal. The mucous membrane of the stomach showed most extensive hemorrhages, large and small, just beneath the surface. The lumen contained a large amount of hemorrhagic fluid. The remainder of the small intestine was filled with dark clotted fluid which stopped rather abruptly at the ileocecal valve. In the region of the transverse colon and rectum other submucous hemorrhages were seen.

Lymph Glands: The lymph glands were examined carefully and did not appear enlarged. The superficial and deep nodes, however, were red and unusually firm.

Brain: The meninges were normal. There was no thrombosis in the sinuses. Over the convexity just beneath the dura was a small collection of fresh blood which might or might not have been there before death. The convolutions were not flattened. No areas of softening were seen. The blood vessels at the base showed extensive arteriosclerotic changes.

Bone Marrow: The bone marrow from the ribs was red. The cavity of the femur, however, contained only a large amount of fat in which an occasional reddish collection of active marrow was seen.

Microscopic Notes (We are indebted for the following careful description to Dr. W. G. McCallum, who kindly reviewed the available material):

Bone Marrow: The sections were made from the bone marrow of the femur which was practically entirely composed of fat. There were, in crevices between the fat globules and around the small vessels, sparse accumulations of cells which at first sight seemed to be all of one type. In sections stained successfully with Wright's stain among these cells no megalocaryocytes were found, no nucleated red cells, no eosinophil myelocytes and only rarely a neutrophil myelocyte of normal appearance. Most of the cells were rather smaller than myelocytes and had relatively large rounded, eccentric nuclei which were sharply outlined and filled with large scattered blocks of chromatin, such as are seen in plasma cells. In this respect they differed from normal myelocytes seen in control sections of bone marrow, since in those cells the nucleus was

more delicately stained, with a clearly defined nucleolus and finely divided chromatin particles. The cytoplasm took a purplish stain, usually without definite evidence of the presence of granules. There was sometimes a pale area about the nucleus. It seemed possible that these cells might be regarded as the basophilic ancestral cells of myelocytes, although they did not correspond with the ordinary descriptions of myeloblasts. A few true myelocytes were discoverable after much search.

It appeared that the bone marrow of the femur at least had ceased entirely to produce the elements of the blood, and any blood formation must be looked for in the bone marrow of the vertebrae and short bones, which was described as red.

Blood formation might also be looked for in the spleen and liver.

Spleen: The spleen was uniform in appearance throughout various sections. The trabeculae, and especially the blood vessel walls, showed rather extensive hyalin changes which became very conspicuous in some sections stained faintly by Wright's stain. The malpighian bodies were rather small but otherwise unchanged. The splenic pulp was fairly full of blood in the sinuses, and there were some extravasations of red corpuscles into the substance. There were numerous minute collections of bacilli in the pulp, surrounded by necrotic cells but by no inflammatory reaction. Between the venules the splenic reticulum contained numerous deeply stained cells exactly resembling those found in the bone marrow. These rather large cells formed conspicuous strands and masses between the venules and were occasionally found within them. Their cytoplasm was basophilic but not distinctly granular, and their nuclei contained abundant large blocks of deeply stained chromatin. They, too, occasionally showed an eccentric pale halo about the nucleus. In most respects they were like plasma cells but they were less regular in form and size and were not obviously and definitely plasma cells.

Liver: The liver showed several large areas of necrosis in each section. These were formed about great masses of bacteria which were chiefly staphylococci, but which were mixed about the edges with abundant bacilli. It will be remembered that in the spleen and kidney only bacilli were found. There was no reaction about the necrotic areas. The tissue in general looked normal so that the bile ducts and portal veins appeared to run in wide bands of connective tissue. This was infiltrated in places with cells which entirely resembled those seen in the splenic pulp. None of these cells were found in the capillaries of the liver lobules.

Kidney: In general the kidney was normal. The epithelium of the tubules was spread apart by dilatation of the convoluted tubules, but it was not markedly degenerated. There were a few scarred areas in which wandering cells were abundant. They had the character of those described in the portal spaces. There were a few small clumps of bacilli with minimal surrounding areas of destruction of the cells.

Lungs: The lungs were extremely edematous, the alveoli being filled with a bloody fluid. Most of the red corpuscles were still visible, but extensive laking seemed to have occurred. There were masses of bacilli scattered everywhere in the alveoli, but there was no pneumonic reaction.

Lymph Glands: The lymph glands were little altered; the lymph cords contained only lymphocytes, and the sinuses were practically empty. There were no large cells like those described. In the mesenteric glands, however, the sinuses contained numerous large phagocytic cells.

DISCUSSION

This case provides confirmatory evidence of points developed in our previous communications.[1] The blood picture is the same as that observed in other cases of stomatitis and of dermatitis exfoliativa. Platelet counts, which were unfortunately lacking in our earlier cases, are provided; they explain the tendency to hemorrhage often noted in cases of this general group. The condition of the bone marrow at necropsy confirms the observation previously made that death may be due to aplastic anemia alone; or, as shown by the absence of inflammatory reaction about the foci of bacteria in the lungs, liver, and spleen, it may result from the destruction of the bodily defense mechanism against bacterial invasion, in which the bone marrow is chiefly concerned.

A careful search of the literature has revealed only three reports of similar cases, aside from those already reported from this clinic.

Labbé and Langlois [2] report the case of a young woman with secondary syphilis, whose treatment consisted of sixteen injections of neo-arsphenamin. The tenth and each succeeding injection were followed by epistaxis and bleeding from the gums, of gradually increasing severity. After the fifteenth injection some purpuric spots appeared on the skin, which increased in severity following the last dose on December 8. Hemorrhages from the nose, gums, and vagina were now severe and the patient died three weeks later. The blood showed the following changes: Red blood cells, 1,601,000; white blood cells, 4,650 (polymorphonuclears 30 per cent., lymphocytes 25, mononuclears 35); coagulation time, nineteen minutes; bleeding time more than one hour. The clot was not retractile. The authors call attention to the blood picture, which they state resembles that of purpura and hemophilia. They believe that the damage was caused by the action of arsenic on the liver.

Eschbach [3] reports a similar fatal case, following the second dose of neo-arsphenamin. The details are scanty.

Two cases are reported by Görke.[4] Both patients were women, of whom one died and one recovered. In one instance the drugs employed were sodium arsphenamin and neo-arsphenamin; in the other, silver arsphenamin. The symptoms were the same in both cases, con-

2. Labbé, M., and Langlois, S.: Purpura hémorrhagique aigu par intoxication arsénicale, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:786, 1919.

3. Eschbach, H.: Contribution au rôle du novarsénobenzol dans les ictères chez les syphilitiques et dans les dyscrasies sanguines, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:1120, 1919.

4. Görke, H.: Auftreten von aplastscher anämie nach Salvarsan, München. med. Wchnschr. **67**:1226, 1920.

sisting of hematemesis, epistaxis, severe skin purpura and necrotic angina. The blood picture was similar to that described in our own case, consisting of anemia, marked leukopenia with an almost complete absence of leukoblastic bone marrow cells and decrease in platelets.

In our opinion, reactions of this type are by no means so rare as the few reports in the literature would indicate. We have shown that damage to the bone marrow, as indicated by changes in the blood picture, is also present in the majority of patients reacting to arsenical drugs, with a rash of the exfoliative dermatitis group, and that these blood changes differ only in degree from the maximally severe reaction, as seen in this case. It has been further demonstrated [5] that the blood changes may be produced to a mild degree by the administration of an arsenical drug without the occurrence of any reaction. We, therefore, regard as closely interrelated the arsenical reactions of dermatitis exfoliativa, stomatitis, itching and purpura, the connecting link being in the similarity of the alterations in the blood.

In a previous paper [1] we laid much stress on the recognition of the prodromal symptoms of reactions of the group, and we enumerated as important the occurrence of itching, a mild macular, maculopapular or vesicular rash, prolonged fever, malaise or any tendency toward purpura. Since the preparation of this material, we have had the opportunity of observing several patients in whom such prodromes occurred. In each instance, a study of the blood revealed a slight decrease in neutrophil cells, eosinophilia from 5 to 8 per cent., a slight increase in the large mononuclear transitional group and the presence of numerous fragile leukocytes. The necessity for caution in further treatment was thus strongly emphasized.

While we have nothing to offer regarding the treatment of these reactions, the means we have suggested for their early recognition on the basis of the blood picture represents a definite step toward the prevention of the more severe forms.

SUMMARY

We present the history of a patient who developed a fatal aplastic anemia after neo-arsphenamin. The literature is reviewed, attention is drawn to the relation of this type of reaction to dermatitis exfoliativa following arsphenamin, and the practical application of early recognition of the characteristic blood changes in the prevention of these reactions is pointed out.

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5. Moore, J. E.: The Action of Arsenicals on the Blood Picture in Man, Exper. Med., to be published.

STUDIES CONCERNING THE INFLUENCE OF ARSENICAL PREPARATIONS ON CUTANEOUS TESTS

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For a long time the medical profession has felt the urgent need of a simple and certain diagnostic test for syphilis. The wide distribution of syphilis, the fact that syphilis can and does simulate many other diseases, and the fact that even experts are at times baffled in their diagnosis, have emphasized the necessity for a simple and certain diagnostic test for this disease.

After von Pirquet announced his reaction for tuberculosis, many investigators, among them Finger, Wolff-Eisner, Nicholas and others, attempted to obtain a specific reaction by applying extracts of syphilitic tissues to the skin of syphilitic patients. Neisser and Meirowsky had found that normal hepatic extract could not only occasionally give a similar exanthematic result as syphilitic extract, but that the test might also give a positive result in patients in whom there was no reason to suppose the existence of syphilis. In spite of some rather encouraging results, the majority of results from this method proved contradictory and disappointing. Both Neisser and von Pirquet expressed the hope and belief that a specific skin test for syphilis could be obtained by employing the extract of *Spirochaeta pallida* free from tissue constituents.

With Noguchi's cultivation of *Spirochaeta pallida,* a new stimulus was given to these investigations. In 1911, Noguchi brought out "luetin" a sterile extract of the spirochete unadulterated by any tissue constituents. Luetin was injected intracutaneously in a dose of 0.07 c.c. diluted with salt solution, or 0.035 c.c. undiluted. The skin of the arm was suggested as the site of injection. In this investigation the luetin of Parke, Davis and Company was employed. The dose was 0.07 c.c. injected intracutaneously into the upper arm. We quote from a personal letter sent us by Parke, Davis and Company which details the method they followed in manufacturing their luetin:

"Pure cultures were allowed to grow for periods of six, twelve, twenty-four and fifty days at 37 C. under anaerobic conditions. One was cultivated in ascitic fluid containing a piece of sterile placenta and the other in ascitic fluid agar also containing placenta. The lower

portion of each solid culture in which a dense growth had occurred was cut out and the tissue removed. The agar columns which contained innumerable spirochetes were then carefully ground in a sterile mortar. The resulting thick paste was gradually diluted by adding, little by little, the fluid cultures which also contained an enormous mass of the pure organisms. The dilution was continued until the emulsion became perfectly liquid. The preparation was next heated to 60 C. for sixty minutes in a water bath and then 0.5 per cent. phenol was added. When examined under a dark-field microscope, 40 to 100 dead *Spirochaeta pallida* per field could be seen."

INTERPRETATION OF REACTION

In our investigation we found that a number of our patients, after receiving luetin injections, showed a small papule devoid of erythema. This was noted twenty-four and forty-eight hours after the test was made, but disappeared subsequently. This type of reaction we considered of negative value.

Two types of positive reactions were observed: (*a*) Papular: This consisted of a large, red, indurated papule which made its appearance in from twenty-four to forty-eight hours after injection, usually attended with a surrounding erythema. In the great majority of our subjects this reaction disappeared at the end of a week. (*b*) Pustular: This type of reaction began as the papular, except that the lesions became edematous looking and at times associated with the development of miliary vesicles. The lesion soon became pustular with crusting and, at times, very slight scar formation. In several instances of this type of reaction the pustular condition persisted for three weeks before healing.

Our investigation had for its aim the determination of these facts:

1. What would be the influence of a repetition of the luetin test and the tuberculin (von Pirquet) test?

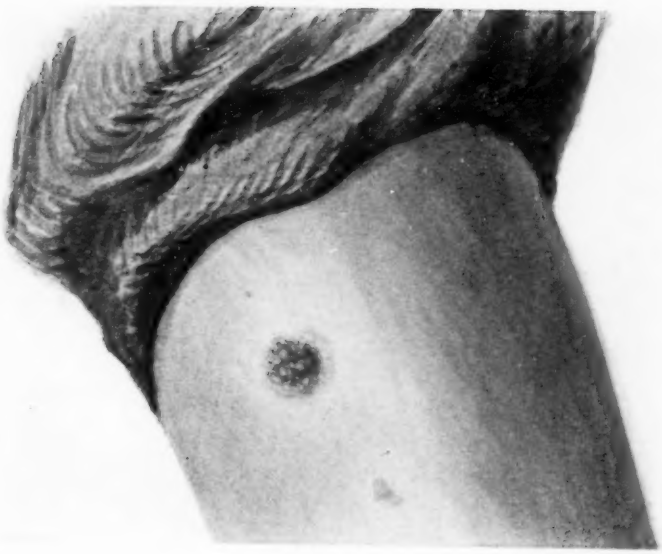
2. What would be the influence of intravenous injections of arsphenamin on the luetin test and the tuberculin (von Pirquet) test?

3. What would be the influence of intravenous injections of cacodylate of soda on the luetin test and the tuberculin (von Pirquet) test?

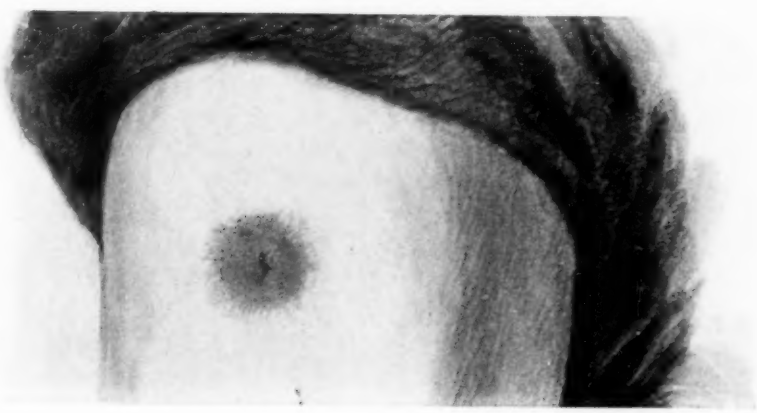
THE INFLUENCE OF A REPETITION OF THE LUETIN TEST

For a study of this problem we selected fourteen patients from the dermatologic dispensary of the Jefferson Hospital. The patients suffered from various skin diseases, principally eczema and acne vulgaris. At least two Wassermann tests were made on each patient, both of which had to be negative before they were selected as eligible for this investigation.

Table 1 shows that in every case the first luetin test was negative, that in the repetition of the test there were three instances out of four-



A, 1 H. P.; second luetin test strongly positive—pustular type obtained after three intravenous injections of arsphenamin. The first luetin test made before the injections were given was negative.



B, 2 B. C.; strongly positive tuberculin (von Pirquet) test following four intravenous injections of arsphenamin. The lesion was about the size of a quarter of a dollar, red and edematous, and surrounded by a number of small vesicles. The first tuberculin test made before the injections were given was negative.

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teen in which the previous negative reaction became positive, and these positive reactions were produced in the absence of any medication. It will also be noted that in all instances but two an interval of three weeks elapsed between the first and second tests.

At this juncture it seems proper to discuss the cause or causes of these positive luetin tests produced by repetition. Among the theories which have been advanced to explain the occurrence of a positive luetin

TABLE 1.—RESULTS OF VARIOUS TESTS

Case	Diagnosis	Number of Wassermann Tests	Result of Wassermann Tests	Result of First Luetin Test	Result of First Von Pirquet	Interval Between Tests, Weeks	Result of Second Luetin Test	Result of Second Von Pirquet Test
1. E. S.	Squamous eczema	3	All Neg.	Neg.	Neg.	3	Marked papule erythma positive	Negative
2. M. M.	Pityriasis rosea	3	All Neg.	Neg.	Neg.	3	Negative	Negative
3. S. P.	Acne vulgaris	3	All Neg.	Neg.	Neg.	3	Marked papule erythma positive	Negative
4. C. R.	Acne vulgaris	3	All Neg.	Neg.	Neg.	3	Marked papule redness positive	Negative
5. C. F.	Acne vulgaris	2	All Neg.	Neg.	Neg.	2	Negative	Negative
6. W. M.	Dermatitis	4	All Neg.	Neg.	Neg.	4	Negative	Negative
7. T. M. C.	Eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative
8. G. R.	Sycosis vulgaris	2	All Neg.	Neg.	Neg.	3	Negative	Negative
9. J. P.	Seborrhea sicca	2	All Neg.	Neg.	Neg.	3	Negative	Negative
10. G. C.	Seborrhea sicca	2	All Neg.	Neg.	Neg.	3	Negative	Negative
11. M. H. B.	Leukoplacia	3	All Neg.	Neg.	Neg.	3	Negative	Negative
12. H. S.	Squamous eczema	11	All Neg.	Neg.	Neg.	3	Negative	Positive marked swelling, redness vesiculation
13. C. A. D.	Eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative
14. A. T. P.	Papular eczema	2	All Neg.	Neg.	Neg.	3	Negative	Negative

reaction in tertiary syphilis is the alleged peculiarity of the cutis of the syphilitic at that stage of the disease which Neisser termed "Umstimmung" of the skin. Can we possibly explain our positive luetin findings produced by the repetition of the luetin test on the ground that the first inoculation of dead spirochetes sensitized the skin of subjects so that the subsequent luetin tests could be capable of producing a positive result? This would appear a logical theory and would agree with the conception of the production of a positive luetin test.

THE INFLUENCE OF INTRAVENOUS INJECTIONS OF ARSPHENAMIN ON THE LUETIN TEST

For this study we selected seventeen patients suffering from various skin affections: acne vulgaris, eczema, psoriasis and other conditions. At least two negative Wassermann reactions were necessary before

the patients were considered eligible for this investigation. A study of this table shows that ten patients received three injections of arsphenamin, three received four injections, two received five injections and one received two injections before the luetin test was repeated.

These injections were given at weekly intervals, the average dose being 0.4 gm. given intravenously. It will be noticed that of this series nine patients gave a positive luetin reaction on repetition, and eight responded negatively to a repetition of the luetin test.

TABLE 2.—RESULTS OF ARSPHENAMIN ON LUETIN TESTS

Case	Diagnosis	Wassermann Report	Number of Wassermann Tests	Result of First Luetin Test	Number of Arsphenamin Injections	Results of Subsequent Luetin Tests
1. B. C.	Purpura	Negative	2	Negative	5	Luetin test, papule and erythema positive
2. I. C.	Acne vulgaris	Negative	2	Negative	3	Negative
3. W. H.	Urticaria	Negative	2	Negative	5	Negative
4. K. P.	Acne vulgaris	Negative	2	Negative	4	Negative
5. F. H.	Acne vulgaris	Negative	2	Negative	5	Positive, papule and erythema
6. H. H.	Urticaria	Negative	8	Negative	3	Negative
7. R. C.	Acne mutilans	Negative	2	Negative	3	Negative
8. E. R.	Acne vulgaris	Negative	2	Negative	2	Positive, marked papule becoming pustular secondarily
9. J. D.	Pityriasis rosea	Negative	2	Negative	5	Slightly positive papule with infiltration and slight erythema
10. O. D.	Acne vulgaris	Negative	2	Negative	4	Positive, papule with erythema
11. G. L.	Acne vulgaris	Negative	9	Negative	3	Negative
12. H. L.	Furunculosis	Negative	2	Negative	3	Positive, papule with erythema
13. G. S.	Folliculitis	Negative	2	Negative	3	Slightly positive papule with slight erythema
14. H. P.	Eczema	Negative	9	Negative	3	Markedly positive pustular type of reaction, see illustrations
15. H. R.	Dermatitis herpetiformis	Negative	2	Negative	3	Negative
16. B. T.	Prurigo nodularis	Negative	2	Negative	3	Markedly positive pustular type
17. R. K.	Psoriasis	Negative	2	Negative	3	Negative

THE INFLUENCE OF CACODYLATE OF SODA, INTRAVENOUSLY ADMINISTERED, ON THE LUETIN TEST

In this series we employed five patients, who fulfilled the same requirements as those in the previous series. These patients received 10 c.c. of cacodylate of soda, intravenously, this solution containing the same amount of arsenic as 0.6 gm. of arsphenamin. It will be noted that of this series only one patient presented a slightly positive reaction. It is to be regretted that this series was small. In addition we performed the luetin test on a series of seven patients who had received from ten to twenty-one injections of cacodylate intravenously at weekly intervals. Of this series one patient presented a marked reaction of the papular type, and in the other instance the papular

reaction was positive but not marked. It is our impression that this last experiment seems to prove the influence of cacodylate of soda on the luetin test.

TABLE 3.—INFLUENCE OF CACODYLATE OF SODA ON THE LUETIN TEST

Case	Diagnosis	Wassermann Report	Number of Wassermann Tests	Result of First Luetin Test	Number of Injections of Cacodylate of Soda	Results of Subsequent Luetin Tests
1. H. N.	Lichen planus	Negative	2	Negative	2	Negative
2. A. S.	Vesicular eczema	Negative	2	Negative	4	Negative
3. E. G.	Eczema	Negative	2	Negative	3	Negative
4. T. J.	Eczema	Negative	3	Negative	3	Slightly positive, papule and redness
5. C. D.	Sycosis vulgaris	Negative	3	Negative	1	Negative

INFLUENCE OF IODIDS AND BROMIDS ON LUETIN TEST

I shall review in brief the influence of iodids and bromids on the luetin test in comparison with the influence of arsenical preparations given intravenously on the same test.

It was shown by Sherrick, and confirmed by others, that nonsyphilitic persons taking bromids or iodids at the time that this skin test is made, or while these drugs are still in the body fluids, may yield well marked nonspecific reactions which may be interpreted as positive luetin reactions. N. C. Borberg, in an exhaustive study of the mechanism of this phenomenon, concludes that the administration of iodin salts produces "Umstimmung" of the skin which is apparent by an increase of the inflammatory reaction around bacterial deposits.

We feel that our study warrants us in stating that arsenic probably produces the same susceptibility of the skin in nonsyphilitic persons, so that the administration of arsphenamin may cause the production of a positive luetin test in nonsyphilitics. In our series we have shown that while the repetition of the luetin test yielded 21 per cent. positive reactions, the arsphenamin series yielded 53 per cent. positive reactions, which is highly suggestive if not conclusive.

It is an obvious step to compare the depot of luetin in the skin with that of the spirochete depot in papules and gummas, and to regard the reaction of the arsenic and also iodin imbibed tissues around the former as a picture of what may be supposed to take place around the latter. We have therefore what we may call an unspecific Herxheimer reaction—an acute aseptic inflammation.

TUBERCULIN INVESTIGATIONS

The Influence of the Repetition of the Tuberculin Test.—In this investigation we also studied the repetition of the tuberculin (von Pirquet) method. Table 1 shows that the tuberculin test in the four-

teen subjects proved negative, while the repetition resulted in one positive result among this series of fourteen patients.

Influence of Intravenous Injections of Arsphenamin on Tuberculin Test.—We then selected another series of ten patients on whom at least two Wassermann tests had been performed and performed the tuberculin (von Pirquet) test on them. We then administered arsphenamin intravenously in a dose of 0.5 gm. at weekly intervals. After our patients had received a certain number of these injections, we again performed the tuberculin (von Pirquet) method with the results shown in Table 4.

TABLE 4.—Influence of Arsphenamin on Tuberculin Tests

Case	Diagnosis	Result of First Tuberculin Test	Number of Injections of Arsphenamin	Result of Subsequent Tuberculin Test
1. B. C.	Purpura	Negative	3	Strongly positive
2. I. C.	Acne vulgaris	Negative	5	Negative
3. Wm. H.	Urticaria	Negative	4	Negative
4. D. K.	Acne vulgaris	Negative	3	Negative
5. F. H.	Acne vulgaris	Negative	4	Weakly positive
6. H. H.	Urticaria	Negative	6	Strongly positive
7. R. C. G.	Acne mutilans	Negative	6	Negative
8. E. R.	Acne vulgaris	Negative	1	Negative
9. D. M.	Pityriasis rosea	Negative	5	Negative
10. H. R.	Dermatitis herpetiformis	Negative	6	Negative

Table 4 shows that except in one instance in which only one injection of arsphenamin was given, the number of injections of arsphenamin varied from three to six; also that of this series of ten patients, two patients showed well marked reactions with distinct swelling, erythema and miliary vesicles, this phenomenon lasting about five or six days before subsiding. In all our work the tuberculin of the H. K. Mulford Company was utilized and in each instance of the test a glycerin bouillon control was made.

The Influence of Intravenous Injections of Cacodylate of Soda on the Tuberculin Test.—In five instances we studied the effect of intravenous injections of cacodylate of soda on the tuberculin (von Pirquet) test. In one instance in which the patient had been gassed in army service, the first as well as the subsequent tuberculin test made after two intravenous injections of cacodylate of soda, proved positive. In the four other instances the first tuberculin (von Pirquet) tests were negative and the subsequent von Pirquet tests after two to four intravenous injections of cacodylate of soda also were negative. Also, without doing a preliminary tuberculin test we performed a von Pirquet test on seven patients, each of whom had received intravenous injections of cacodylate of soda varying from ten to twenty treatments, and in every case but one the tuberculin tests were negative. That one showed a weak positive von Pirquet reaction.

From this study we may conclude that arsphenamin injections are capable of sensitizing the skin to such an extent that it can change the mechanism of the tuberculin (von Pirquet) test so that a positive result can be obtained.

It would appear to us that the arsphenamin acted with the tuberculin test in the same way as the arsphenamin acted with the luetin test.

N. C. Borberg, in his study of the luetin test and the effects of the iodin preparations on it, also tested the effects of the iodin preparations on the tuberculin test, and he found that the iodids were capable of influencing the tuberculin (von Pirquet) test, producing at the point of inoculation a sort of local Herxheimer reaction; hence it would appear that arsphenamin acts in the same way as the iodids both in the luetin and tuberculin tests.

It may be possible that this "Umstimmung" of the skin produced by arsphenamin may account for the influence which Stokes found arsphenamin possesses in the treatment of various forms of tuberculosis of the skin.

In an investigation which we are conducting it appears that neither the intravenous injections of arsphenamin nor that of cacodylate of soda have any influence on the anaphylactic food tests made either by the intracutaneous or the scratch methods.

CONCLUSIONS

As a result of our studies we may conclude:

1. The repetition of a luetin test in nonsyphilitic patients is capable of producing positive luetin tests in about 21 per cent. of our subjects.

2. The intravenous administration of arsphenamin apparently stimulates the production of a luetin test in nonsyphilitic patients, and in our series we were able to produce 53 per cent. positive luetin tests following this form of intravenous specific therapy.

3. In our experience the intravenous administration of cacodylate of soda acts in the same manner as arsphenamin, only more feebly.

4. The repetition of the tuberculin (von Pirquet) test may produce a positive finding, but very infrequently, occurring only once in our series of fourteen subjects.

5. The intravenous administration of arsphenamin is capable of producing a positive tuberculin (von Pirquet) test, previously negative. This occurred in three instances in our series of ten patients.

6. The anaphylactic food test made by either the endermic or scratch method does not seem to be influenced by the intravenous administration of either arsphenamin or cacodylate of soda. Our investigation of this phase of the problem is, however, not yet complete.

7. We are now engaged in studying the effect of the arsenicals given by mouth on the luetin, tuberculin and anaphylactic food tests.

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EXPERIENCES WITH SODIUM ARSPHENAMIN (DIARSENOL)

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MINNEAPOLIS

Sodium arsphenamin was introduced in the early part of 1915 and was used in large quantities in Germany. Favorable reports have been made by Dreyfus,[1] Fabry and Fischer,[2] Gutmann,[3] Hoffmann,[4] Loeb,[5] Seyfarth,[6] Wechselmann,[7] Brandweiner,[8] Hirsch,[9] Schmitt,[10] Ylppö [11] and Glombitza.[12]

LITERATURE

With the exception of one preliminary report,[13] all of the literature on this subject is confined to the German.

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2. Fabry and Fischer: Ueber ein neues Salvarsan-Präparat: "Salvarsan-Natrium," München. med. Wchnschr., No. 18, p. 612-614 (May 4) 1915.

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5. Loeb, Heinrich: Salvarsannatrium, Deutsch. med. Wchnschr., No. 12, p. 335-336 (March 18) 1915.

6. Seyfarth: Ueber die Verabreichung von konzentrierten Salvarsan-natriumlösungen, München. med. Wchnschr. **62**:1707 (Dec. 7) 1915.

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8. Brandweiner, A.: Ueber Salvarsannatrium nebst einigen allgemeinen Bemerkungen zur Salvarsantherapie, Wien. klin. Wchnschr. **29**:10 (Jan. 6) 1916.

9. Hirsch, Hans: Ueber Salvarsannatrium, München. med. Wchnschr., No. 27, p. 964-966 (July 4) 1916.

10. Schmitt, Artur: Erfahrungen mit Salvarsannatrium in konzentrierte Lösung, München. med. Wchnschr. **63**:270, 1916.

11. Ylppö, A.: Salvarsan-Natrium behandlung der Lues congenita, Therap. Monatschr. **32**:155-165 (May) 1918.

12. Glombitza: Salvarsan-Natrium als intravenöse Injektion in hochkonzentrierter Lösung, Deutsch. med. Wchnschr., No. 21, p. 646-648 (May 24) 1917. Spätexantheme nach Salvarsan-Natriuminjectionen, No. 46, p. 1452-1453 (Nov. 15) 1917.

13. Wright, F. R., and Michelson, H. E.: Experience with Sodium Diarsenol, Arch. Dermat. & Syph. **2**:499 (Oct.) 1920.

Dreyfus,[1] in 1915, reported on the results of 450 injections. He used the drug in combination with mercury in cases of cerebrospinal syphilis and obtained good results. He rarely gave over 0.45 gm.

Fabry and Fischer,[2] after using various doses and dilutions, decided that from 0.3 gm. to 0.6 gm. (average, 0.45 gm.) in 50 c.c. of water was the best dosage. They thought the drug could be used in more concentrated solution. They gave from three to five injections in a series at a four to five day interval. They do not report any marked reactions.

Gutmann[3] gave 1,538 injections to 175 patients. The drug was dissolved in 30 c.c. freshly distilled water, independent of the dose. He started with from 0.15 gm. to 0.3 gm. and gradually increased the dosage to 0.6 gm. In a few cases he gave as high as 0.75 gm. without obtaining any reactions. In a single course the highest total amount given a man was 7.5 gm. in forty-four days, in a woman 6.5 gm. in fifty-five days and in a 6-year old child 3.3 gm. in fifty days. Injections were made at four-day intervals. He did not report any serious reactions, but noted these symptoms: (1) a rise of temperature to 38 C. in 4.4 per cent. of the cases; (2) nausea, vomiting, headache, diarrhea, occasionally; (3) no albuminuria in patients treated with sodium arsphenamin; (4) the angioneurotic syndrome in two patients; (5) exanthem in ten patients (eight women and two men).

From the clinical standpoint, he found that spirochetes disappeared in twenty-four hours, and the syphilitic lesions regressed rapidly. He came to the conclusion that this drug approaches old arsphenamin in its therapeutic efficiency.

Hoffmann[4] reported the results of 1,500 injections in 242 patients. The dosage in men was from 0.45 gm. to 0.6 gm. and in women from 0.3 gm. to 0.45 gm. Injections were given at from five to seven day intervals. (The smaller doses were given only at the beginning and at the end of a long course.) The drug was dissolved in freshly distilled 0.4 per cent. saline solution in the proportion of 0.1 gm. of the drug to from 10 to 20 c.c. of the saline solution. Only two patients showed severe reactions.

Loeb[5] found that roseola and papules disappear in one week after one injection and condylomas in two or three weeks. He treated ninety-four patients. A 5½ year old congenital syphilitic patient took 0.3 gm. without bad results. He concluded that this drug is as non-toxic as neo-arsphenamin and its therapeutic activity lies between arsphenamin and neo-arsphenamin.

Seyfarth[6] used a concentrated solution (0.45 gm. in 1 c.c. of water) without any bad effects.

RESULTS OBTAINED WITH SODIUM ARSPHENAMIN THERAPY

Patient's Number	Clinical Manifestations	Laboratory Data	Number of Injections Patient Received	Number of Injections Necessary to Remove Lesions	Wassermann Reaction After First Course	Wassermann Reaction After Second Course	Remarks
863	Chancre	Spirochetes + Wassermann +	8 (0.6 gm.) biweekly	3	Negative		
17514	Chancre	Spirochetes + Wassermann +	3 (0.4 gm.) 3-day interval	2	Negative	Negative after 2 months	Disappeared for 2 months after 3 injections
836	Chancre	Spirochetes + Wassermann +	2 courses 8 (0.4 gm.) each	2	Negative	Negative	
18250	Chancre; papular eruption	Wassermann +	6 (0.4 gm.) biweekly	5	Negative		
16804	Chancre	Spirochetes + Wassermann —	8 (0.6 gm.) weekly	3	Negative	Negative	
17314	Chancre; macular eruption	Wassermann +	8 (0.4 gm.) biweekly	2			
15438	Tabes	Blood Wassermann —	8 (0.3 gm.) biweekly	...	Negative (spinal fluid)	.....	No change
922	Chancre	Spirochetes + Wassermann —	5 (0.4 gm.) biweekly	1	Negative		
921	Follicular syphilid; chancre 12 years ago	Wassermann +	5 (0.4 gm.) weekly	2	Negative		
931	Alopecia	Wassermann +	1 (0.6 gm.)	...	.....	.....	Disappeared after first injection
16925	Chancre; roseola	Spirochetes + Wassermann +	8 (0.4 gm.)	1	Negative		
596	Tabes	Wassermann —	8 (0.6 gm.) weekly	...	Negative	.....	No change
818	Chancre	Wassermann +	8 (0.4 gm.) biweekly	2	Negative		
749	Gumma on clavicle	Wassermann +	2 (0.4 gm.) biweekly	...	Positive	.....	Disappeared after second injection
16454	Chancre	Wassermann —	8 (0.6 gm.) biweekly	3	Negative	Negative	
16674	Chancre	Spirochetes +	8 (0.3 gm.) biweekly	1	Negative		
106552	Aortitis	Wassermann +	6 (0.4 gm.) weekly	...	Positive	Positive	
796	Tabes	Blood Wassermann —	8 (0.6 gm.) weekly	...	Negative	Negative	
856	Chancre; macular eruption	Spirochetes — (4 times) Wassermann +	8 (0.6 gm.) biweekly	2	Positive	Negative	
7636	Cerebrospinal syphilis	Spinal fluid Wassermann +, blood Wassermann —	8 (0.4 gm.) biweekly	...	Blood Wassermann —, spinal fluid Wassermann +	.....	No improvement
811	Gumma palate; perforated septum	Wassermann —	14 (0.6 gm.) weekly	Improved after first	Positive after 1 month's rest	.....	Marked improvement in general health

904	Alopecia	Wassermann +	1 (0.6 gm.)	Gradual	.....	.....	Disappeared after first injection
659	Wife has syphilis; asymptomatic syphilis	Wassermann +	8 (0.6 gm.) weekly	...	.....	.....	No further report
6465	Asymptomatic syphilis	Wassermann +	6 (0.6 gm.) weekly	...	Positive after 6 weeks' rest		
797	Alopecia; mucus patches; macular eruption; papula on uvula	Wassermann +	7 (0.6 gm.) weekly	3	Negative		
813	Chancre	Wassermann —	8 (0.45 gm.) biweekly	1	Negative	.....	Gained 10 pounds
847	Papular eruption; alopecia of eyebrows	Wassermann +	7 (0.3 gm.) biweekly	Gradual	Positive		
927	Meatal chancre; squamopapular eruption	Wassermann +	5 (0.4 gm.) biweekly	3	Negative		
917	Macular eruption	Wassermann +	8 (0.6 gm.) biweekly	2	Negative after 3 weeks' rest	.....	General improvement
915	Chancre	Spirochetes + Wassermann —	4 (0.6 gm.) biweekly	2	Negative	.....	Special note
15351	Palmar syphilid	Wassermann +	8 (0.45 gm.) biweekly	3	Positive after 3 weeks	Positive	
878	Chancre	Wassermann +	11 (0.4 gm.) biweekly	1	Negative after 3 weeks' rest	Negative	
313	Papules on penis; general macular eruption	Wassermann +	3 (0.4 gm.) biweekly	2	Negative after 12 administrations of mercury		
315	Chancre	Spirochetes + Wassermann +	2 (0.4 gm.) in 2 days	1	Negative after 12 administrations of mercury		
16557	Macular eruption	Wassermann +	6 (0.4 gm.) biweekly	2	Negative		
946	Chancre; macular eruption	Wassermann +	2 (0.4 gm.) biweekly	2	Negative		
857	Chancre	Spirochetes + Wassermann +	5 (0.6 gm.) biweekly	2	Negative	.....	Left city
814	Asymptomatic syphilis	Wassermann +	13 (0.6 gm.) weekly	...	Positive after 6 injections		
914	Chancre; papular eruption	Spirochetes + Wassermann +	8 (0.6 gm.) biweekly	3	Negative	Negative	
932	Chancre	Wassermann +	4 (0.6 gm.) biweekly	2	Negative after 12 administrations of mercury		
913	Gumma on tibia	Wassermann +	4 (0.4 gm.) weekly	3	Negative		
936	Chancre	Wassermann —	5 (0.4 gm.) biweekly	1	Negative		
780	Chancre	Wassermann +	8 (0.6 gm.) weekly	2	Negative after 4 weeks' rest	Positive after 10 weeks' rest	
884	Chancre	Spirochetes + Wassermann —	8 (0.4 gm.) biweekly	1	Negative		
16367	Chancre	Spirochetes —	7 (0.4 gm.) biweekly	7	Negative		
15995	Maculopapular eruption	Wassermann +	6 (0.45 gm.) biweekly	3	Negative		

RESULTS OBTAINED WITH SODIUM ARSPHENAMIN THERAPY—(*Continued*)

Patient's Number	Clinical Manifestations	Laboratory Data	Number of Injections Patient Received	Number of Injections Necessary to Remove Lesions	Wassermann Reaction After First Course	Wassermann Reaction After Second Course	Remarks
17002	Ulcer on tonsil; macular eruption	Wassermann +	8 (0.6 gm.) weekly	1	Positive		
17228	Chancre	Wassermann +	8 (0.45 gm.) biweekly	8	Positive after third injection		
17672	Chancre; macular eruption	Wassermann +	6 (0.6 gm.) biweekly	3	Positive (?)		
18049	Macular eruption; mucus patches	Wassermann +	5 (0.6 gm.) weekly	3	Positive		
18240	Chancre on lip	Spirochetes +	7 (0.4 gm.) biweekly	5	Negative		
		Wassermann +					
18246	Alopecia; ulcer on tongue	Wassermann +	6 (0.6 gm.) biweekly	5	.....	.....	Left city
14738	Alopecia	Wassermann +	4 (0.6 gm.) biweekly	After 4th dose hair stopped falling out	Negative after 12 administrations of mercury		
15669	Papular eruption	Wassermann —	10 (0.6 gm.) biweekly	4	Negative	Negative	
15224	Papular eruption	Wassermann +	7 (0.6 gm.) biweekly	2	Negative		
15206	Papule on tongue and lower lip	Wassermann +	12 (0.3 gm.) weekly	1	Positive after 6 weeks' rest		
14985	Pustular eruption; chancre	Wassermann +	8 (0.6 gm.) biweekly	3	Negative after 6 weeks' rest		
15770	Chancre	Wassermann —	12 (0.6 gm.) biweekly	1	Negative after 3 weeks' rest		
14856	Papule on tonsil; papule on glans	Wassermann —	8 (0.6 gm.) biweekly	2	Negative after 3 weeks' rest		
15607	Chancre 2 months old	Wassermann +	5 (0.6 gm.) biweekly	2	.....	.....	Disappeared
16457	Papule on forehead; mucus patches	Wassermann +	8 (0.45 gm.) weekly	3	.....	.....	Disappeared
1593	Interstitial keratitis; adult congenital lues	Wassermann —	3 (0.6 gm.) 3 days	Disproved after 3	Negative	.....	Improvement not marked
1612	General macular eruption; periostitis of frontal bone	Wassermann +	4 (0.4 gm.) biweekly	4	.....	Negative after 24 administrations of mercury	Special note
1614	Palmar syphilid; gumma of wrist	Wassermann +	3 (0.6 gm.) in 3 days	2	Positive	.....	Marked improvement. Left city
1618	Tabes; tabetic bladder	Wassermann —	5 (0.4 gm.) 2-day intervals	5	Negative	.....	Marked improvement
1624	Serpiginous ulcerating lesion of the chest	Wassermann +	2 (0.4 gm.) in 2 days	Slow healing	Positive	Positive after 12 administrations of mercury	Improved rapidly when changed to mercury treatment
261	Chancre	Wassermann —	3 (0.45 gm.) in 3 days	Healing after 1st injection	Negative		
		Spirochetes +					

Wechselmann [7] reported the results of 12,000 injections. He gave from 0.3 gm. to 0.45 gm. twice a week, giving a total of from forty to fifty doses, without mercury. He had only two exanthems and no other severe reactions. He found that high concentration was inadvisable.

Brandweiner [8] reported 298 injections in 189 fresh cases. After experimenting with various doses and dilutions he recommends 20 c.c. of water independent of dosage. He gained the impression that it was somewhat more toxic than neo-arsphenamin and therapeutically equal to either of the other drugs.

Hirsch [9] found that sodium arsphenamin is an excellent, strongly acting preparation.

Schmitt [10] reported on ninety-seven injections. He found it advisable not to use over 0.45 gm., and the dose was dissolved in 10 c.c. of water. Injections were made at eight-day intervals. He obtained no cutaneous reactions and concluded that sodium arsphenamin is easier and safer to give than old arsphenamin, but no more active.

Ylppö [11] used the drug intravenously in congenital syphilis. He gave from 0.07 to 0.1 gm., repeating from twenty to thirty-five times; he followed the cases from nine to eighteen months and observed a lasting effect.

Glombitza [12] used sodium arsphenamin in highly concentrated solution and had no reactions worthy of note. He reported in a later communication an exanthem coming on several weeks after a course of treatment. His conclusions are in accord with those of other observers.

MODE OF ADMINISTRATION

All of the injections were made intravenously with a Luer syringe of 10 c.c. capacity. The drug was dissolved in sterile, freshly distilled water. We first used a 20 c.c. dilution irrespective of this dosage, but soon concentrated the solution to 10 c.c. without any untoward effect. We used the drug in three ways:

(*a*) Three moderate doses (from 0.45 to 0.6 gm.) were given at twenty-four or forty-eight hour intervals, followed by twelve mercuric salicylate (0.5 c.c.) injections.

(*b*) Eight moderate doses (0.45 gm.) were given at three day intervals; no mercury was used in this group.

(*c*) A weekly moderate dose (0.6 gm.) was given for periods varying from eight to twelve weeks. Mercury was not used in this group either.

MATERIAL

A total of 545 injections was made on sixty-six patients (twenty-two with primary syphilis, thirty with secondary syphilis, nine with tertiary syphilis, and five with neurosyphilis). In all cases the patients were ambulatory and no preliminary precautions, such as an empty

stomach, atropin injections or purge, were employed. The patient, in many instances, returned immediately to his occupation, which often was physical labor.

All of the patients showed active lesions or symptoms of syphilis when the sodium arsphenamin therapy was instituted.

REACTIONS

We encountered no severe reactions resulting from injections of sodium arsphenamin. Chills and fever following the first injection, in florid cases, were almost a constant observation. Vomiting and diarrhea occurred occasionally within the first twenty-four hours. Dizziness was noted, but we had no case of syncope or collapse. Headache was complained of by a few patients.

We saw few retarded reactions. There was no case of jaundice. Dermatitis was noted twice, once rather severe, but not severe enough to result in an exfoliative dermatitis. Two patients who gave dermal reactions to neo-arsphenamin also gave dermal reactions to minute doses of sodium arsphenamin.

Anorexia and loss of weight were not noted. Perivenous infiltration, which occurred in a few cases, caused about the same degree of pain and swelling as observed with neo-arsphenamin. (Many of these injections are made by senior students.)

There were a few cases which we deem of sufficient interest to report in detail, because they emphasize certain phases.

REPORT OF CASES

Results Obtained with Sodium Arsphenamin Therapy

Case 780.—A man, aged 26, single, with a chancre on the shaft of the penis, enlarged lymph nodes, and a positive Wassermann reaction, received eight doses of sodium arsphenamin, 0.6 gm., at weekly intervals. He rested three weeks and the Wassermann test remained negative. He developed smallpox and was isolated for six weeks, when he returned. The Wassermann reaction had reverted to positive. We believe that had mercury been administered following the sodium arsphenamin course the Wassermann reaction would have remained negative.

Case 915.—Another case which demonstrated the need of supplementing the sodium arsphenamin course with mercury was Case 915. A man, aged 30, presented himself with a chancre; the dark field was positive; the Wassermann reaction was negative. He received six injections of 0.6 gm. sodium arsphenamin, the first three biweekly and the next three weekly. He was out of the city for six weeks. When he returned, he had a recurrent papular eruption with a positive Wassermann reaction.

Case 1612.—A girl, aged 18, presented a generalized macular eruption, severe throat lesions and hypertrophied papules on the vulva. The Wassermann reaction was positive. She received four injections of 0.4 gm. sodium arsphenamin at four-day intervals. She did not report for two months, when she pre-

sented herself because of a severe unilateral facial paralysis which responded to antisyphilitic treatment. The Wassermann reaction at that time was still positive.

CASE 15206.—A woman, aged 22, presented herself with papules on the tongue and lower lip, general adenitis and a positive Wassermann reaction. She received four weekly doses of 0.4 gm. of sodium arsphenamin. She then rested six weeks when the Wassermann reaction was negative. She was then given a second series of six weekly doses of 0.3 gm. After the second and fifth injections she suffered from severe gastric distress. After the second gastric reaction, she was given two weeks' rest and the sixth injection was made with neo-arsphenamin (Metz), 0.3 gm. A similar reaction occurred. Mercury was ordered for subsequent treatment. This case shows that a reaction may not be due to a particular form of arsphenamin.

CASE 106552.—A man, aged 32, with aortitis, had previously received twenty-six injections of neo-arsphenamin, thirty-six injections of mercury, and sixty mercury rubs. The Wassermann reaction was persistently positive. He was given six injections of sodium arsphenamin, 0.4 gm., weekly. The Wassermann reaction remained positive throughout. He complained of severe gastric upset and depression throughout the course.

COMMENTS

Sodium arsphenamin offers the physical and therapeutic features of arsphenamin in convenient form. It is difficult, from a clinical experience, to arrive at an accurate determination of the relative value of the various arsphenamins. Suffice it to say that sodium arsphenamin exerts a marked effect on cutaneous and mucous membrane lesions of syphilis, and that this action is almost as rapid and profound as when arsphenamin or neo-arsphenamin is employed.

The dosage employed by us was small. Marked effect was produced on lesions with 0.3 gm. given to males of approximately 150 pounds' weight. From our observations, we believe that 0.45 gm. is a safe and efficient dose, and we noted that doses of 0.6 gm., although borne without severe reactions, nevertheless produced a certain effect on the patient, which patients described as, "makes me feel sort of tired" or "I'm kind of grippy."

We used a dilution of 20 c.c. with the first doses given. This dilution was gradually and cautiously decreased to 10 c.c. No change in effect or safety of administration was noted.

We found that a course of six doses of from 0.3 gm. to 0.6 gm. made an optimum course. Injections subsequent to six doses often produced minor symptoms of intolerance (gastric distress, itching sensation).

Injections were made daily for three doses; injections were made every forty-eight hours for three doses; biweekly injections for six doses and weekly injections for six doses were made without any symptoms which we could attribute to the interval. We believe that in all arsphenamin courses the patient must be carefully watched and

questioned for early warning symptoms on the part of the organism against arsenic, and that the slightest significant symptom should cause the operator to delay subsequent injections in order to avoid accumulative effect. We have not observed a case of exfoliative dermatitis which was the result of an initial dose of any of the arsphenamins. Our cases of dermatitis have occurred after repeated doses, and when we have carefully questioned the patient afterwards, we have discovered minor symptoms which we did not heed at the time, making our subsequent injection in spite of the warning, with a resulting dermatitis. We wish to call particular attention to two such minor symptoms: first, itching, which appears shortly after injection and lasts for from twelve to twenty-four hours. We have learned to accept this as a distinct warning to lengthen the period between injections and to lower the dose. Second, substernal or epigastric, dull, but persistent, pain.

Constant use of the arsphenamins breeds contempt. Operators make light of the injection; patients speak in jocular terms of their "shot"; and they exhibit a bravado when in groups at a clinic which causes them to conceal, or at least not to mention, minor symptoms. These factors cause one to overlook the gravity of the occasion and the dangers which are lurking in antisyphilitic treatments. The responsibility rests with the operator, and we believe that many of the minor and major effects of arsenic intolerance can be avoided by a carefully regulated dose and interval.

We most emphatically believe that sodium arsphenamin does not possess any qualities which permits the omission of supplemental treatment with mercury.

Sodium arsphenamin does not change a positive Wassermann reaction to negative any faster, or slower, than any of the other arsphenamins we have used. We believe that this change is to a large degree dependent on the age of infection at the time treatment is instituted and on individual response to a certain amount of therapy.

CONCLUSIONS

1. Sodium arsphenamin is a readily soluble, easily administered and safe preparation.

2. Sodium arsphenamin exerts a marked influence on clinical manifestations of syphilis.

3. We believe that courses of sodium arsphenamin should be supplemented with mercury.

4. The therapeutic efficiency is apparently equal to that of the other arsphenamins (clinically).

5. The effect on the Wassermann reaction is about on a par with that of the other arsphenamins.

A REVIEW OF THE LITERATURE AND A DISCUSSION OF SILVER ARSPHENAMIN *

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Silver arsphenamin, the latest of the arsphenamin series of drugs, is now on the market, and is being used in America. There is no English literature to guide one in determining its qualities. Our communication is an effort to review the literature on silver arsphenamin and to draw conclusions therefrom.

Silver arsphenamin was suggested by Ehrlich, whose untimely death cut short his researches, which were continued by Kolle who finally elaborated silver arsphenamin. This drug was first used clinically in March, 1918.

Kolle,[1] in 1918, in the first of a series of articles, gives the following table which shows that silver arsphenamin had a more profound effect on experimental syphilis than any of the other members of the arsphenamin group. He concludes from his work that silver when combined with the arsphenamin molecule forms a combination which has a greater spirocheticidal action than other combinations with which he worked.

In his second article, published in 1919 Kolle,[2] discusses at length the chemical properties of the drug and concludes that silver arsphenamin acts on the syphilitic process in a two-fold manner: The arsphenamin molecule exerts its well-known spirocheticidal effect, while the presence of the silver radical seems to inhibit the growth of the spirochetes. Therefore, he says, silver arsphenamin acts in combination.

Kolle,[3] in 1920, reviewed the clinical results of various observers.

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1. Kolle, W.: Experimentelle Studien zu Ehrlich's Salvarsan therapie der Spirochätenkrankheiten und über neue Salvarsanpräparate, Deutsch. med. Wchnschr. Nos. 43 and 44, p. 1177, Oct. 24, 1918 and Oct. 31, 1918.

2. Kolle, W., and Ritz, H.: Experimentelle Untersuchungen über die Wirkung des Silbers und seiner Verbindungen auf die Kaninchensyphilis, mit besonderer Berücksichtigung des Silbersalversans, Deutsch. med. Wchnschr. No. 18, 1919.

3. Kolle, W.: Weitere Mitteilungen über Silbersalvarsan, Deutsch. med. Wchnschr. No. 2, 1920.

Fabry,[4] in 1918, used silver arsphenamin on 100 patients, all of whom had active clinical manifestations of syphilis. At first he hospitalized his patients, but later he used the drug on ambulatory cases. He dissolved 0.2 gm. in 5 c.c. of sterile distilled water, and later 0.3 gm. in 6 or 7 c.c. using a 10 c.c. syringe. He found that infiltration of the subcutaneous tissues with a solution of this concentration was very painful. He concluded that 0.2 or 0.3 gm. of silver arsphenamin is sufficient to cause the disappearance of spirochetes from the lesions; that sclerosae and condylomas disappear, at least as rapidly as with old arsphenamin, and that large tertiary ulcers involute with great rapidity. No bad effects were noticed. There was a slight febrile reaction in "secondary syphilis" after the first injection. He noticed urticarial reactions in some cases, which disappeared in a few days. He did not repeat injections until all signs of dermal reaction had

Effect of Various Drugs on Experimental Syphilis

Drug	Therapeutic Dose	Spirochetes Disappeared After
Old Arsphenamin	0.01 gm. per kilo	72 hours
Neo-Arsphenamin	0.015 gm. per kilo	48 hours
Copper Arsphenamin	0.004 gm. per kilo	96 hours
Gold Arsphenamin	0.005 gm. per kilo	48 hours
Platinum Arsphenamin	0.005 gm. per kilo	48 hours
Silver Arsphenamin	0.004 gm. per kilo	24 hours

subsided. The Wassermann reaction did not revert to negative as quickly as one would expect from a drug whose clinical action was so rapid and intense.

In 1919, Fabry,[5] after further extensive use of silver arsphenamin, stated that he believed it to be the most active of the arsphenamin products on clinical manifestations and for destruction of spirochetes. At the same time, the necessary dosage is decidedly smaller than that of any of the other products. In order to determine the tolerance for the drug, he employed heroic treatment using from 0.2 to 0.3 gm. at three to four day intervals, giving ten to twenty doses. Later he decided that he obtained the same clinical results with a longer interval —five to seven days. With regard to the action on the Wassermann reaction: It became negative in many cases, but in active secondary syphilis it often remained positive. For this reason, he recommended

4. Fabry, J.: Ueber die Behandlung der Syphilis mit Silbersalvarsan, Deutsch. med. Wchnschr. No. 44, p. 1216-1218, Oct. 31, 1918.

5. Fabry, J.: Ueber Behandlung der Syphilis mit Silbersalvarsan, Deutsch. med. Wchnschr., No. 49, p. 1358-60, Dec. 4, 1919.

that a few neo-arsphenamin and mercury injections be given following a course of silver arsphenamin. He reported a case of universal weeping dermatitis after two injections (0.1 and 0.2 gm.); the patient recovered promptly.

Galewsky,[6] in 1918, gave 700 injections of silver arsphenamin to 165 patients. The injections were given after working hours on ambulatory patients. He considers silver arsphenamin a powerful drug whose therapeutic dose is one-third that of old arsphenamin, but whose toxic dose is two and one-half times as great as neo-arsphenamin. He always used it in combination with mercury, giving ten to fourteen mercury and four to eight (0.1 to 0.15 gm.) silver arsphenamin injections for the first course, and six to eight mercury and two to four silver arsphenamin injections for the subsequent courses. He gave weekly or biweekly injections, and noted no ill effects. The Wassermann reaction became negative as often and as early as with any other arsphenamin preparation.

Galewsky,[7] in 1920, after giving 2,000 injections, decided that the best average dose for women was 0.2 gm. and for men 0.25 gm., eight to fifteen injections constituting a course. Results were more rapid than with old arsphenamin. Spirochetes could not be found from twenty-four to forty-eight hours after the first dose. Sclerosae and roseolae disappear in a few days. The Wassermann reaction becomes negative very often after three weeks or after 1.5 to 2.0 gm. of the drug have been given, and he emphatically states that it reverts to negative more rapidly than with any other arsphenamin preparation. He concludes that silver arsphenamin takes the first place in the treatment of early syphilis and in effecting abortive "cures." In the treatment of early tabes, vascular and cerebral syphilis, special care must be exercised in using silver arsphenamin. He believed that there are fewer untoward effects with silver arsphenamin than with any of the other arsenical preparations. Finally, he belives the time has come to decide definitely in which group of cases a pure arsphenamin treatment should be instituted, and whether it is not advisable to give up the combined mercury and arsphenamin courses.

Gennerich,[8] in 1918, gave 1,000 injections of silver arsphenamin to 100 patients. Small doses, from 0.1 to 0.2 gm., were given at four day intervals until four doses had been given; then the interval was lengthened to six or seven days until the course of five to ten injections

6. Galewsky, E.: Ueber Silbersalvarsannatrium, Deutsch. med. Wchnschr. No. 48, pp. 1326-1327, Nov. 28, 1918.

7. Galewsky, E.: Zwei Yahre Silbersalvarsan-Therapie, München. med. Wchnschr. Jan. 30, 1920.

8. Gennerich: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 45, pp. 1243-1244, Nov. 7, 1918.

had been completed. He believes that the drug is the most powerful and the safest of the arsphenamin preparations, having only four minor reactions in his entire series. Furthermore, he believes that the drug is especially suitable for the abortive "cure of primary Wassermann negative cases." A patient with this type of case he treated for from two and one-half to three weeks after first excising the chancre. He thinks courses of silver arsphenamin are more efficient in fresh secondary syphilis than courses of any other arsphenamin product or than courses of arsphenamin combined with mercury.

In 1919, Gennerich [9] again reported on the results of 3,500 injections of silver arsphenamin on 315 patients. As the war had caused a scarcity of silver arsphenamin, some of his courses had to be supplemented with injections of neo-arsphenamin. In these cases he did not give more than seven injections of neo-arsphenamin because of the danger of icterus. In 3,500 injections of silver arsphenamin, he saw only one case of mild icterus.

Hahn,[10] in 1918, gave 1,000 injections of silver arsphenamin to eighty-two patients. He treated both recent and old cases of syphilis, and was in accord with the opinion of other observers that cutaneous and mucous membrane lesions disappeared rapidly. His observations on old cases of syphilis are especially interesting. He noted that in a series of Wassermann-fast cases, the reaction soon became negative and remained negative for the length of the period of observation. He reports no severe reactions, and states his hope that this drug will eliminate the need of mercury in the treatment of syphilis.

Hahn,[11] in 1920, reported his further observations on silver arsphenamin, having given 4,000 injections to 300 patients. He standardized his technic beginning with 0.1 gm. and gradually increasing the dosage to 0.3 gm. given biweekly, in from 10 to 20 c.c. of sterile distilled water. The Wassermann reaction always became negative after twelve injections in fresh cases and almost always in old cases. He concluded that the action of silver arsphenamin on all the manifestations of syphilis in all its stages is excellent and that it acts rapidly and with certainty.

Hugo Miller,[12] in 1918, gave 1,000 injections of silver arsphenamin to 170 patients. He thinks that silver arsphenamin sterilizes the human

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9. Gennerich: Kriegserfahrungen in der Luesbehandlung, unter besonderer Berucksichtigung des Silbersalvarsans, Berl. klin. Wchnschr., p. 769, Oct. 18, 1919; No. 34, p. 803, Oct. 25, 1919.

10. Hahn, F.: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 50, pp. 1385-1386, Dec 12, 1918.

11. Hahn, F.: Silbersalvarsan in der Syphilistherapie, Deutsch. med. Wchnschr. No. 4, pp. 92-93, Jan. 22, 1920.

12. Miller, Hugo: Silbersalvarsannatrium-Behandlung der Syphilis, Deutsch. med. Wchnschr. No. 51, pp. 1415-1416, Dec. 19, 1918.

organism infected with syphilis more thoroughly than any other drug which we have. He also thinks that the effect on the Wassermann reaction is more noticeable than with neo-arsphenamin. Dermal reaction can be avoided by slow injection with great dilution.

Sellei,[13] in 1918, observed that secondary lesions were not immediately affected, but that a few days after injection there was rapid involution. In a case of nephritis with syphilis he gave the drug without ill effects. Sellei,[14] in 1920, found that dosage of 0.04, 0.06, 0.08 and 0.1 gm. gave the same results as 0.1, 0.15, 0.2 and 0.3 gm., and affected the Wassermann reaction sooner. He believes the drug is particularly suited for use in syphilis of the nervous system.

Weichbrodt,[15] in 1918, used the drug in eighteen cases of paresis and tabes. He thought the drug suitable, but drew no conclusions. There was no marked effect on paresis.

Weichbrodt,[16] in 1919, noted that three months after the spinal fluid had been made negative with silver arsphenamin it became positive, and he tried in vain to revert it to negative. His final conclusion was that silver arsphenamin is the drug of choice in paresis, although it gives no permanent benefit to the patient.

Hauck,[17] in 1919, reported on 600 injections into sixty patients in all stages of syphilis. He started with 0.1 gm., gradually increasing the dose to 0.25 gm. for women and 0.3 gm. for men. He gave from ten to twelve doses in a course, and did not use mercury in combination. One injection of 0.1 gm. was sufficient to cause disappearance of mucous patches. The effect of a course of silver arsphenamin was particularly striking in its effect on the lymph node enlargement. The adenitis disappeared rapidly. He found definite improvement in tabes after twelve injections of 0.1 gm. There were no severe reactions, exanthems or icteri, and he concluded that silver arsphenamin is a great advance in the therapy of syphilis.

Kerl,[18] in 1919, used the drug in concentrated solution, 0.1 gm. in 6 c.c. of water, and concluded that the same result can be obtained with

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13. Sellei, J.: Das Silbersalvarsan, Deutsch. med. Wchnschr. No. 45, pp. 1247-1248, Nov. 7, 1918.

14. Sellei, J.: Weitere Erfahrungen mit Silbersalvarsan, Med. Klin. No. 12, Mar. 21, 1920.

15. Weichbrodt, R.: Silbersalvarsannatrium und Sulfoxylatpräparat (No. 1495) in der Paralyse-therapie, Deutsch. med. Wchnschr. No. 44, pp. 1216-1217, Oct. 31, 1918.

16. Weichbrodt, R.: Weitere therapeutische Versuehe bei Paralyse, Deutsch. med. Wchnschr. No. 13, pp. 357-358, Mar. 27, 1919.

17. Hauck, L.: Die Behandlung der Syphilis mit Silbersalvarsannatrium, Med. Klin. No. 24, pp. 581-582, Jan. 15, 1919.

18. Kerl, W.: Ueber Silbersalvarsan, Wien. klin. Wchnschr., 1919, No. 17, pp. 446-447.

0.1 to 0.2 gm. of silver arsphenamin that one can obtain with 0.4 gm. of old arsphenamin.

Knopf and Sinn,[19] in 1919, treated eighty-two patients with active manifestations. They treated fifty-nine with silver arsphenamin only; in twenty-three cases they combined its use with mercury. Their objections to the drug were:

1. It is hard to see undissolved particles.

2. It is more difficult to determine an oxidized product than in the case of lighter colored arsphenamin.

3. It is hard to see blood in the syringe when aspirating after venipuncture.

Their technic was to administer 0.1 gm. on the first day, 0.2 gm. on the third or fifth day, and after that 0.3 gm. every fourth day for ten or twelve injections. They encountered angioneurotic reactions when they used concentrated (5 to 10 c.c.) solutions. These disappeared on using 15 to 20 c.c. of dilutant and making very slow injections. They concluded that the effect on the Wassermann reaction is not as great as would be expected in view of the intense action on clinical manifestations.

Kreibich [20] in 1919, gave 400 injections to 100 patients, using 0.2 to 0.3 gm. in two to four doses in a course. He gave 0.2 gm. to a weak 8-year old boy twice within ten days with beneficial effect and no reaction. He used a 10 c.c. dilution, noting only mild reactions. On active lesions, 0.3 gm. of silver arsphenamin gives about the same result as 0.4 gm. of old arsphenamin. Spirochetes begin to disappear in six hours, and are all dead (in the dark field) in twenty-four hours. Considering the arsenic content, he believes silver arsphenamin is more desirable than old arsphenamin.

Sinn,[21] in 1919, reported a fatal case of hemorrhagic encephalitis in a man 21 years of age with florid secondary syphilis, who received three doses of silver arsphenamin. The first dose consisted of 0.15 gm.; three days later he received 0.25 gm., and four days later 0.25 gm. He also received seven injections of mercury and one injection of mercury salicylate. Two days after the last silver arsphenamin injection, he became unconscious and died three and one-half days later, in spite of all efforts.

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19. Knopf, W., and Sinn, O.: Ueber Silbersalvarsan nebst Bemerkungen über Konzentrierte Altsalvarsan-einspritzungen, Deutsch. med. Wchnschr. No. 19, pp. 517-518, May 8, 1919.

20. Kreibich, C.: Ueber Silbersalvarsannatrium, Med. Klin. No. 7, Feb. 16, 1919.

21. Sinn, O.: Ueber Neurorezidive nache reiner. Salvarsan und Silbersalvarsanbehandlung, München. med. Wchnschr. No. 43, pp. 1228-1229, Oct. 24, 1919.

Lenzmann,[22] in 1919, gave 250 injections of silver arsphenamin. He used a more dilute solution than most of the observers, 0.1 to 0.25 gm. in 20 to 40 c.c. He decided that the drug was suitable for use, and was well borne and less toxic than the other members of the arsphenamin group. The technic of injection, he thought was more difficult because of the color of the solution. The action on spirochetes was rapid. The drug was well borne by children. He had had reactions in two patients which lasted for a few days; they were characterized by substernal pain and stridulous breathing and a croupous cough. Both patients recovered. Concerning the effect on the Wassermann reaction, he thought it was too early to make a definite conclusion.

Lenzmann,[23] in 1919, used silver arsphenamin in a case of aortitis, but made no special comment on its value in this type of syphilitic involvement.

Levy-Lenz,[24] in 1919, gave seventy injections of silver arsphenamin. He had no severe reactions. He used a concentrated solution, 0.1 gm. in 3 c.c. of sterile distilled water, and he did not believe that slow injection was essential, or that the darkness of the fluid made injection more difficult, for aspiration when the needle was paravenous gave air bubbles, and when intravenous the volume of fluid in the syringe increased.

Von Notthaft,[25] in 1919, thought that the drug is the equal of old arsphenamin, but insisted on dilution and slow injection using 120 c.c. of water and a gravity apparatus. He obtained angioneurotic symptoms when he used concentrated solutions. He did not think it advisable to use silver arsphenamin simultaneously with mercury. He had given silver arsphenamin steadily for a period of six months and even longer without ill effect, and he believed that the solution is stable for at least thirty minutes.

Riecke,[26] in 1919, reported a death occurring in a man 41 years of age, who had a ten-week old case of florid syphilis. He was otherwise normal. He received 1.3 gm. of silver arsphenamin in seven injections over a period of forty-two days. After the first injection of 0.2 gm. he had fever, chills and weakness lasting several hours. The

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22. Lenzmann, R.: Ueber Erfahrungen mit Silbersalvarsannatrium, Deutsch. med. Wchnschr. **45**:355-357 (March 27) 1919.

23. Lenzmann, R.: Uber Aortitis luica, Ztschr. f. ärztl. Fortbild. No. 23, 1919.

24. Levy-Lenz: Meine Erfahrungen mit Silbersalvarsan, Deutsch. med. Wchnschr. **45**:1440-1441 (Dec. 25) 1919.

25. Von Notthafft: Erfahrungen mit Silbersalvarsan, Deutsch. med. Wchnschr. **45**:341 (Mar. 27) 1919.

26. Riecke, E.: Schwere Erscheinungen nach Silbersalvarsan in einem Falle florider Syphilis, Med. Klin. No. 14, pp. 329-330 (April 6) 1919.

interval was five days. Headache and exaggeration of his first symptoms followed the third and fourth injections of 0.2 gm. The fifth injection of 0.15 gm. brought forth no symptoms of intolerance, but after the sixth injection of 0.15 gm. he had a facial erythema. In spite of this warning, he received a seventh injection of 0.2 gm. ten days later, which was followed by a severe generalized dermatitis and a complicating bronchopneumonia which terminated fatally. Riecke insisted that this death was due to intoxication with silver arsphenamin and that the drug alone was at fault.

Rille and Frühwald,[27] in 1919, gave ninety-two patients the usual dosage and remark that the drug is well tolerated. There were no ill effects, but its action on the Wassermann reaction was irregular.

Zieler,[28] in 1919, reported a case of severe generalized dermatitis following an injection of silver arsphenamin.

Buschke,[29] in 1919, observed two neurorecidives after initial courses of silver arsphenamin.

Carl Stern,[30] in 1919, gave 1,000 injections to ambulatory patients. His technic was unusual in that he dissolved the drug in a small amount of water and, after venipuncture, he aspirated considerable blood allowing the solution and the blood to mix before injection. He says that Kolle advised him that addition of serum lowered the toxicity of the drug. He also gave a few intramuscular injections which were surprisingly well borne, with very little pain.

Fritz Kalberlah,[31] in 1919, treated nine patients with multiple sclerosis with good results, which he remarks may be due to the well-known remissions in this condition.

Deutsch,[32] in 1919, observed four patients with negative Wassermann reactions in whom spirochetes were found. Each was given three doses of 0.3 gm. of silver arsphenamin at four day intervals. No further treatment was administered, but they were observed each month for one year, and they had neither a clinical nor a serologic relapse. In a fifth case of primary syphilis in which the Wassermann

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27. Rille, J., and Frühwald, R.: Die Behandlung der Syphilis mit Silbersalvarsannatrium, München. med. Wchnschr. No. 43, p. 1226, Oct. 24, 1919.

28. Zieler: Würsburger Aertzeabend 17 **6**:19, 1919. München. med. Wchnschr., No. 29, 1919.

29. Buschke: Berl. Dermat. Geo. 13 **5**:19; Deutsch. med. Wchnschr. **69**:435, 1919.

30. Stern, C.: Die Technik der Silbersalvarsaninjektion, München. med. Wchnschr. No. 48, p. 1377, 1919.

31. Kalberlah, F.: Die Behandlung der multiple Sklerose mit Silbersalvarsannatrium, Med. Klin. No. 32, 1919.

32. Deutsch, R.: Abortivbehandlung der Syphilis mittels Silbersalvarsan, Dermat. Wchnschr. **69**:1919.

reaction was positive, he gave a total of 1.2 gm. of silver arsphenamin. The Wassermann reaction promptly became negative and remained so throughout the year of observation without further treatment.

Delbanco,[33] in 1919, treated sixty ambulatory cases with good results and no marked reactions.

Hoppe,[34] a neurologist, in 1919, treated twenty patients with neurosyphilis. He gave both intravenous and intramuscular injections of silver arsphenamin. The intramuscular injections were not very painful, and the local reaction caused passed away rapidly for in a week neither physician nor patient could tell on which side the previous injection had been given.

Schönfeld and Birnbaum,[35] in 1919, reported the use of silver arsphenamin for one year on sixty-seven patients, 1,000 injections being given. They concluded that its action on clinical manifestations is rapid; that silver arsphenamin surpasses neo-arsphenamin and sodium-arsphenamin; it about equals old arsphenamin and is less toxic. Its action on lymphadenitis is remarkably swift. The effect on the serology was found to be variable. Mild reactions were more frequent with silver arsphenamin than with old arsphenamin, but prolonged reactions were not encountered. In retrospect, after a year's use, they recommend that mercury still be combined in the therapy of old syphilis.

Goldberger,[36] in 1919, gave 266 injections to sixty patients. He reported no bad effects, but he believes that we should persist in the combination of mercury with arsphenamin. Since silver arsphenamin is more active than neo-arsphenamin and less toxic than old arsphenamin, Goldberger thinks that the change is very desirable, but if there is the slightest warning of intolerance, it should be discontinued at once.

Bruhns and Löwenberg,[37] in 1919, reported the results of 1,000 injections on 107 patients. Spirochetes disappeared in sixteen hours after the injection of 0.1 gm. They summarize the results on the Wassermann reaction: "Fifty-five strongly positive cases at the beginning of the course, forty-nine were negative at completion." They

33. Delbanco, E.: Zum Silbersalvarsan und zur Biologie der Menschen und Kaninchensyphilis, Deutsch. med. Wchnschr. **45**:150 (Feb. 6) 1919.

34. Hoppe, J.: Ueber Silbersalvarsannatrium, München. med. Wchnschr. No. 48, p. 1376, 1919.

35. Schönfeld, W., and Birnbaum, G.: Ueber Silbersalvarsannatrium mit besonderer Berücksichtigung des Verhaltens der Wassermann Reaktion. München. med. Wchnschr. No. 38, p. 1087, Sept 19, 1919.

36. Goldberger, P.: Unsere Erfahrungen mit Silbersalvarsan, Med. Klin. No. 38, 1919.

37. Bruhns, C., and Löwenberg: Ueber Silbersalvarsannatrium und die Dosierung des Salvarsans nebst Mitteilung eines Falles von Encephalitis haemorrhagica nach Neosalvarsan, Berl. klin. Wchnschr., 1919, No. 39, p. 913, No. 40, p. 948.

observed slight exanthems and icterus frequently, but always after repeated doses, which emphasizes the necessity of giving the larger doses at longer intervals to avoid accumulative effect.

Dreyfus,[38] in 1919, reported only on purely neurologic cases. He had given 691 injections to sixty-three patients. His initial dose was 0.05 gm. to test the tolerance of the patient; he gradually increased the dose to 0.25 gm. given every second or third day. In his opinion, the drug is especially valuable in early cerebrospinal syphilis, the subjective symptoms disappearing rapidly and the objective symptoms receding in two to three weeks. In the majority of cases there is distinct improvement.

Dreyfus,[39] in 1919, in his second communication, dilated on the various reactions. He classifies them as follows:

1. Anaphylactic—angioneurotic syndromes. This is an immediate reaction which passes off rapidly. He did not see a severe one.

2. Fever usually follows the first injection and is probably due to "endotoxin" liberation.

3. Cutaneous manifestations are urticarial or exanthematous. Dreyfus observed only six exanthems in 1,000 injections.

4. Syncope, collapse, headache, weakness, nausea and vomiting do occur, but he believes this "shock" type of reaction is due to too large initial dosage. He has never observed any alarming or lasting symptoms following this type of reaction.

5. Icterus in his experience is negligible for he merely mentions the possibility of its occurring.

6. Thrombophlebitis—he has not seen this in his series of cases.

Nolten,[40] in 1919, reported on 500 injections in fifty cases. He experienced no difficulties and concludes that silver arsphenamin is the most energetic and least toxic antisyphilitic remedy of the present day.

Ludwig Stern-Piper,[41] in 1920, reported on the use of silver arsphenamin in multiple sclerosis. He concludes that there is some improvement which is apparently not due to the ordinary remission.

Abimelich,[42] in 1920, in a short report comments favorably on the use of the drug.

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38. Dreyfus, G. L.: Silbersalvarsan bei luetischen Erkrankungen des Nervensystems, München. med. Wchnschr., No. 31, pp. 864-869, 1919.

39. Dreyfus, G. L.: Nebenwirkungen des Silbersalvarsans, Deutsch. med. Wchnschr. Nos. 47 and 48, p. 1293, Nov. 20, 1919 and Nov. 27, 1919.

40. Nolten: Silbersalvarsan, Deutsch. med. Wchnschr. No. 36, 1919.

41. Stern-Piper, Ludwig: Beitrage zur Therapie der multiplen Sklerose mit Silbersalvarsan, München. med. Wchnschr., Aug. 20, 1920.

42. Abimelich, R.: Ueber Silbersalvarsan, Deutsch. med. Wchnschr. No. 10, pp. 267-268, Mar. 4, 1920.

Lochte,[43] in 1920, in an article entitled "Argyrie nach Zwölf Silbersalvarsan Injecktionen" relates a case of argyria (?) which he himself did not see. A representative of "Der Naturheilkunde" (nature healer) sent him the following case report which he thought should be published in order to warn his colleagues of the danger of argyria following injections of silver arsphenamin. Lochte, however, remarks that it cannot be verified that the case was argyria. The "nature healer" sent this report to Lochte:

A female, aged 31, infected in March, 1917, received seven neo-salvarsan injections (dose and method not given). All phenomena of lues completely disappeared in eight weeks. She suffered from a relapse in January, 1920, when she first consulted the "Nature Healer," who made a diagnosis of: (1) nodular syphilide of hairy scalp, (2) gummatous periostitis of right tibia, (3) ulcerating syphilide of right arm. Since he did not treat venereal disease, she was referred to a "specialist." (He does not state whether or not the specialist was a dermatologist.) In February, 1920, she returned to the "Nature Healer" with this story: She had reported to the specialist who had given her twelve injections of silver salvarsan. The first dose of 0.2 gm. was given intramuscularly. (The interval or size of subsequent doses was not given.) Five days after the first injection she noticed jaundice which lasted fourteen days. The treatments were not discontinued because the patient felt so well. On March 2, 1920, she noticed an ashen gray discoloration of the skin which rapidly increased.

There was no further observation of the patient. Lochte brings up the question of arsenical pigmentation caused by previous treatments with neo-arsphenamin and asks "What becomes of the silver after silver arsphenamin injections?"

COMMENT

After a careful survey of the literature and as a result of a limited personal use (250 ampules), we feel that we may safely state that silver arsphenamin is an efficient spirocheticide, which has a pronounced effect on the visible lesions of syphilis. It is not surprising that the effect on the Wassermann reaction is variable. The effect of all of the antisyphilitic remedies is variable in their action on this phenomenon. The personal factor must be considered; and since the same person cannot receive two drugs under precisely the same circumstances (age of infection, etc.), it is impossible to make an accurate comparison. Suffice it to say that the consensus of opinion of the many observers is that in the majority of cases of fresh syphilis a positive reaction becomes negative after the first course of from six to ten injections of silver arsphenamin.

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43. Lochte: Argyrie nach Zwölf silbersalvarsan Injecktionen, Therap. Holb. Monatsh. **34**:334, June 15, 1920. Since preparation of this review three American contributions have appeared.

We note that the technic of solution and injection is perplexing to some operators. Because of the brown color of the solution, it is impossible to see undissolved particles. We have found that silver arsphenamin, being a heavy salt, immediately sinks when sprinkled on the surface of its solvent. If two beakers are used, the fluid may be gently decanted from one to the other, and when no residue is left in the bottom of the first beaker, the solution is ready for injection unless one wishes to use a filter. We encountered no difficulty in seeing the blood on aspiration after venipuncture. By using a Luer syringe with a long glass nozzle, the red blood can easily be seen passing through the lumen of the nozzle. There is considerable variation in the optimum dosage. An initial dose of from 0.05 to 0.1 gm. for a person of average weight is best—with a routine dose of from 0.2 to 0.25 gm. Many of the physicians, however, used 0.3 gm. with impunity. Solution in from 10 to 20 c.c. of water appears to be the strength of solution chosen by most of the observers. We are often warned of the necessity of making slow injections, and that the more dilute the solution the less the danger from reaction. Since Kolle advised the mixture of aspirated blood with the solution in order to reduce the toxicity (a fact which he ascertained by animal experimentation), we believe it should be the accepted technic: Dissolve the necessary dose in 10 c.c. of sterile distilled water, draw into a 20 c.c. Luer syringe, make venipuncture, aspirate about 10 c.c. of blood, and reinject the entire solution slowly. We have infiltrated 1 c.c. of such solution paravenously to note the effect. It was decidedly less painful than a like amount of sodium arsphenamin, and passed off more rapidly.

There is no difficulty in detecting an oxidized product. It is necessary to make up the solution first. The perfect product makes a rather sparkling, clear, dark brown solution. A spoiled product has a dull, muddy, grayish brown appearance.

One of the distinct advantages is the absence of the characteristic, and often nauseating, garlic-like or ether-like, odor which patients detect when they are receiving the other arsphenamins intravenously. This odor has made it impossible, or at least impracticable, to administer arsphenamin to certain patients. We administered three doses of 0.1 gm. of silver arsphenamin to such a type of patient. She made no complaint, and said she could detect no odor.

The interval of choice is from four to seven days, and the number of doses in a course varies greatly.

The majority of observers are not in favor of using silver arsphenamin and mercury simultaneously. In our clinic we always complete a course of any of the arsphenamin products before beginning a course of mercury. We can see no advantage of the mixed plan of

administration, and believe that one has less control of either drug when they are given together. Furthermore, in case of ill effect, it is difficult accurately to lay the blame.

Concerning reactions: There is apparently no reaction due to silver arsphenamin which is peculiar to that drug and has not been noticed with any of the arsphenamin group, with the possible exception of argyria, which we shall discuss later.

Angioneurotic symptoms pass off rapidly. Many observers think that this type of disturbance is due to too large an initial dose, a too concentrated solution or too rapid injection. All of this may be avoided by a diluted small initial dose, slowly injected.

Fever is noted after the first injection in florid syphilis, as with other members of the arsphenamin group.

Cutaneous manifestations, if urticarial, pass off rapidly. If the manifestations are exanthematous, they are a warning of intolerance, and should be a positive indication for cessation of arsphenamin therapy, at least for a long period (three to six months); arsphenamin should be resumed only with the greatest caution. Riecke's case of death is an example—in our opinion—of not heeding a distinct warning by the organism against further arsenic. In our experience with exfoliative dermatitis following any of the arsphenamins we noticed a decided intolerance. One patient who developed a severe dermatitis after three doses of neo-arsphenamin (0.6 gm.) at weekly intervals had a decided exanthem from 0.06 gm. given four months later, with complete rest from treatment in the interim.

Syncope, collapse, headache, weakness, nausea and vomiting is the type of reaction which we used to see frequently when we first began using the American made arsphenamins. We noted this type of reaction almost constantly after using certain control numbers. They were promptly discarded as toxic products. Possibly this type of reaction, when noted after the use of silver arsphenamin, was due to toxic chemical by-products which unavoidably occurred in early manufacture.

Icterus is a dangerous complication and requires a careful diagnosis as to cause. Is it due to the drug or to syphilis? Few observers lay much stress on the occurrence of icterus after the use of silver arsphenamin.

Thrombophlebitis was not recorded by any observer.

No authentic case of argyria has been reported! Lochte's report is unfortunate. He did not see the case himself—the case was related to him by a "nature-healer" who did not treat the woman, but who had sent her to a "specialist." She had previously received neo-arsphenamin therapy. During her course of silver arsphenamin she developed icterus, but in spite of this, the treatment was continued,

and if the dates in the report are accurate, she received twelve doses of silver arsphenamin in less than a month's time. Kolle distinctly advises against more than 2.0 gm. in one month. Von Notthaft states that he has continued a course of silver arsphenamin for over six months without ill effect. If argyria were a common danger, one should expect to hear of it in the practice of a man who believes in continuous prolonged silver arsphenamin therapy. Lochte, in his report, suggests that the woman may have had a melanosis due to arsenic, but unfortunately she was not examined by one competent to decide.

Hemorrhagic encephalitis is reported once, but does not differ from similar cases following arsphenamin treatments.

In conclusion, we must repeat that we believe silver arsphenamin is a drug which has a marked effect on the clinical manifestations of syphilis, when administered in smaller doses than is the custom with the other arsphenamins. Whether the effect is more profound and sterilization more thorough will require a longer period of observation to determine. Immediate reactions are about the same as with the other arsphenamins, and it is too early to speak with certainty of remote dangers.

One must constantly bear in mind that silver arsphenamin is a more complex salt than any of the other arsphenamins, and the physician must be on the alert for the slightest sign of intolerance. Its superiority over the other members of the group certainly is not so marked that a patient should in any way be jeopardized in order to receive this drug in preference to the other arsphenamin products.

Although the drug is highly recommended by neurologists, nothing conclusive has been published indicating a selective action on neurosyphilis. It may be that the future treatment of syphilis will call for courses of the various arsphenamin products, each having its relative chronologic position.[44]

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44. In addition to the references given, the following may be of interest: Parounagian, M.: Preliminary Report of Silver Arsphenamin, Arch. of Dermat. & Syph. **3**:333, (March) 1921.

Goodman, Herman: Silver Arsphenamin: Personal Experiences with the German Product, Urol. & Cutan. Rev. **25**:128, (March) 1921.

Walson, C. M.: Silver Salvarsan in the Treatment of Syphilis, Am. J. Med. Sc. **161**:418 (March), 1921.

THE CREAM OF A YEAR AT BEIRUT

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Beirut, despite its isolation, offers peculiar advantages for the study of dermatology. It is on "the bridge of the world"—a connecting link to the continents of Europe, Asia proper and Africa. Its coastal summers are tropical in their heat and humidity; the high mountain ranges, with a delightful climate, are close to the humid coast; and a dry plateau occupies the interior, thus giving a wide variety of climate in a small area. Again, there is a great mingling of peoples and races and customs. Further, the American University of Beirut's School of Medicine has long been recognized as a center of medical teaching in the Near East, and its dermatologic polyclinic has been the first, and for years the only one, in this part of the world. The Kasr al Ainy government medical school at Cairo and the French Jesuit Medical School at Beirut have no dermatologic department or service, and so naturally cases of dermatoses gravitate to the American University of Beirut.

The year 1920 was in some respects remarkable, especially for the number of unusual and rare cases that came under observation, and I feel it a duty to have them put down in black and white. I have called them the "cream of a year," and perhaps I may mention that the whole amount of the "milk" was 6,261 cases, divided into polyclinic cases 3,371 and private cases 2,890. The main portion of the "skimmed milk" consisted, as in all dermatologic work, of eczema, scabies and syphilis, with the impetigos and tineas crowding close. At one period during the war scabies made up about half of my cases. In these statistics there were 1134 cases of scabies, 18.1 per cent. of all, divided into 725 clinical and 408 private cases; eczema totaled 1022 cases, or 16.3 per cent.—548 in clinic and 474 private. Eczema rarely makes up 25 per cent. of the cases in Beirut. There were 340 cases of syphilis, 5.4 per cent.—184 in clinic and 156 private cases. This represents a great falling off from war times.

I shall enumerate the cases of the diseases worthy to be classed as the cream of the year.

SKIN DISEASES IN BEIRUT

There were only three cases of acne rosacea, one clinical and two private. It is not common in Syria. It is so striking that a mistake in diagnosis is hardly possible; but I did have the rare

fortune to see two cases of acne variolformis, one clinical and one private. Actinomycosis gave one clinical case. It is about as rare here as in the United States. I had never expected to see a case of ainhum unless I journeyed to the tropics of Africa, perhaps to see my students in the Sudan; but what was my joy to see two cases of this rare disease at Beirut last year, one case in private practice and the other in the clinic. Both patients were white people. The man had lesions on his toes, the woman on her fingers. Only one case of angioma was seen in my office and one case of alopecia universalis was observed, and that at the clinic. Blastomycosis cutis is relatively common in Syria; no less than eight cases were seen, equally divided between clinic and private practice. There were eight patients with carbuncle, all but one of them in private practice. There were four cases of cheilitis exfoliativa, one clinical and three private.

I am inclined to agree with Schamberg that colloid degeneration of the skin is not so rare a disease as the textbooks would lead us to believe. My two cases last year were private ones, and they are not the first I have seen here in Syria.

There was one case of Darier's disease—a private case; and one case of defluvium unguium in private practice; there were two cases of dengue rash in the same category. We have not had a severe epidemic of dengue in several years in Syria; the sporadic cases are common in the late summer. Not every patient has the typical rash—in fact, I would say that the rash is rather exceptional.

Among the uncommon dermatoses, there were six cases of dermatitis exfoliativa, two in the clinic, and four in the office. Dermatitis herpetiformis is a common malady in Syria; there were thirty-four cases, twenty in the clinic and fourteen in private work. Two cases of dermatitis exfoliativa neonatorum were seen at the clinic, and they were both probably fatal. I had eight cases of dermatitis repens; they were all characteristic. I have found a 1 per cent. solution of potassium permanganate constantly applied to be the best remedy.

There was one case of dermatolysis that would be a fortune-maker for a dime museum. The lesion was on the back—in fact, it occupied all of the skin on the patient's back.

Of thirteen cases of elephantiasis seven patients came to the polyclinic and six to my office. The legs were involved in all. There were fourteen cases of epidermophyton, eight in the clinic and six in office practice. I believe that epithelioma is not as common in Syria as in America. There were thirteen cases, four in clinic and nine in private work. There were nine cases of erythema nodosum, seven clinical and two private. The four cases of that relatively rare fungus disease, erythrasma, were all in private practice.

I recorded four cases of fibroma and four of Fordyce's disease, in each case one in the clinic and three in private practice. There were three cases of gangrene (spontaneous), two in the clinic and one in private work. I saw one case of herpes iris lesion—granted that it is a form of erythema multiforme—yet so uncommon are the Saturnlike rings that I felt it deserves recording as a separate entity. I had the pleasure of demonstrating it to my students at my polyclinic.

I had one case that I call, for want of a better name, herpes meningiticus. The patient was in the hospital suffering from cerebrospinal meningitis, and I was called in to treat the skin lesions. They were generalized, herpetic, and unlike anything in my experience. There were fourteen cases of herpes zoster, six in the clinic and eight private cases.

Hydroa estivale is common in Syria, and it is one of my "betes noirs." There were no less than twenty-two cases of it, equally divided between public and private practice.

All three cases of ichthyosis were seen in the clinic. There were two cases of iodism in private practice.

There were seven cases of keloids—five clinical and two private cases. One developed in a lady's chest after removing a wart with monochloracetic acid. We had two patients with keratosis palmaris et plantaris, but neither patient felt that he could afford to take roentgen-ray treatment for it. Both were clinical cases.

A most curious lesion is that of lentigo circumscripta—two cases of it were seen in the clinic. It is hard for Americans to realize how Syrians hate freckles in any form. I see a great many cases of this blemish, as well as of chloasma.

There were only three cases of lepra during the year—two clinical and one private, whereas before the war I used to average about one new case of it a month. It would seem that many lepers died during the hardships and starvation of the war. Leukoderma is fairly common and yet greatly feared in Syria, for the common name for it in Arabic is "baras," which is one of the vulgar names for leprosy. Many patients fear that it is really lepra, even when most solemnly assured that it is not. Of the seventeen patients, nine came to the clinic and seven to my house. There were five cases of leukoderma et melanoderma syphilitica—three at the clinic and two I saw privately. Two patients with leukoplakia came to my office. This is another class of patients that rarely come to the clinic, as the disease is found mostly in the well-to-do, and I have difficulty in getting patients to demonstrate to my students. I have had striking results in treating the disease with balsam of Peru; it is difficult to apply, but it turns the

trick. There were fifteen cases of lupus erythematosus, six at the clinic and nine at my office. Three cases of lipoma were seen, one in the clinic and two in private practice. I have classed lupus vulgaris with tuberculosis cutis, and it will be discussed later.

There were ten cases of moluscum contagiosum, six at the clinic and four in the office. It is a curious fact that in my first nine years of practice of dermatology in Syria I did not see one case of this lesion, and I was about to publish the statement that it seemed to be absent from this part of the world—in fact, I made this statement to my class when lecturing on it—and most curiously that same day a patient with this disease appeared in my office and two more before the week was out; but in my first ten thousand cases I did not find a single little mollusk!

One clinical and one private patient had onychomycosis. Oriental button, commonly called in Syria the Aleppo button, or the papule of a year, as translated from the Arabic, before the war was rather restricted to certain cities and towns—rife in Aleppo—but during and since that terrible upheaval it has become widespread and generally endemic. I believe that the troops are largely responsible for this great scattering of the disease. Here I wish to protest at calling the lesion a "boil." My friend, the late Dr. Stelwagon, at my request kindly cut out the term "boil," for the lesion has only the shape of a boil to give it that name, and that shape is retained only throughout a portion of its career. True, the term "button" smacks of French nomenclature, yet it is distinctive and for a large part of the time it answers well the description. It is a "sore" only in its last stages. I have records of 193 cases of it last year, 113 were polyclinic and 80 private cases. During the past year we began treating cases by intravenous injection of tartar emetic, in addition to my method of thorough congelation with carbon dioxid snow, which I am convinced is the most rapid and best cure. I had the privilege of discovering that treatment in January, 1910, and have used it ever since, except during some months during the war when carbon dioxid gas was not to be had in the city. I expect to publish some data on this method in the near future.

A little girl came to my office with bathing suit nevus. The concomitant hypertrichosis made it a real "bathing suit." Only one case of nevus flammeus was seen at the clinic. People are only slowly learning what can be done for this disfigurement by carbon dioxid snow. There were fifteen cases of pigmented nevus, six clinical and nine private cases; but not a single case of nevus pilosus. In fact, the Syrians admire a hairy nevus—especially on the face. The men shave all about one, but never cut the hair on the mole, but twist and curl it till it stands out from the face at great length.

Pellagra is disappearing in Syria. It was a scourge during the war, especially among the Turkish soldiers and in the hospices and orphanages for children. I saw only eight cases of it last year, seven at the clinic and one in my office.

Of the difficult forms of pemphigus, there were six cases—two of foliaceous pemphigus, one at the clinic and one at the office; two of pemphigus neonatorum, one at the clinic and one at the office; and two of pemphigus vulgaris—one at the clinic and one at the office. I find it hard to understand the controversy over pemphigus neonatorum and how it can be mistaken for syphilis or could ever be called "impetigo contagiosa bullosa," as some would have us regard the disease.

I had eleven cases of pityriasis rosea of Gibert, six at the clinic and five in my consulting room. The only patients we had last year with pityriasis rubra pilaris, or lichen ruber acuminatus, came to the clinic. (I had a clinical case of it the day that I am writing this paper. But it cannot be included in last year's record!)

Our only patient with porokeratosis came to the clinic. It is the second I have seen here. The patient we had last year had the lesion on her foot. There were two cases of progressive pigmentary dermatosis (Schamberg's disease), one at the clinic and one at my office. The two patients with prurigo nodularis (making three cases in my experience) came to my consulting room. One of them gave me the rare privilege to study the disease in its incipiency, and I found it indeed a most interesting study. Of psoriasis, I had three varieties: eleven cases of vulgaris at the clinic and twenty-two at my office. For the first time I saw psoriasis nigra, and had three cases of it—two at my office and one at the clinic, and the student explaining and reporting on it made the correct diagnosis, though he felt loath to report it as he realized how rare is this variety. At the clinic we had one case of psoriasis verrucosa. There were seven cases of purpura, two clinical and five private.

We saw one case of quinine erythema at the clinic and two at my office.

Only one case of sarcoma was seen; this patient came to the clinic. Only ten cases of sycosis appeared, two in the clinic and eight in private observation. This is more than I ordinarily see here. I do not understand why sycosis should be so relatively rare in this land. Staphylococci are abundant enough for other lesions.

The Syrians tattoo their hands or arms almost as commonly as sailors; but they seldom repent of it and wish the marks removed. I had only two cases of it last year. The patients came to my office and said they wished to be rid of their dermal inscriptions. Of

twenty-eight cases of tuberculosis cutis, in which I have included lupus vulgaris, twenty-five were clinical cases and only three were private cases.

Urticaria is too common to appear in this list, but I think it is worth recording that we had at the clinic one case of giant urticaria and two of hemorrhagic urticaria. The ulcus epidemicum, which invaded Syria in 1917, produced 111 cases, fifty-one were seen at the clinic and sixty at my office. The suffering was so great that, although the disease nearly always attacks the poorer classes, they would be willing to do anything to be healed. I hope later to send some notes on this disabling disease of the skin. There were five cases of xanthoma palpebrarum, one clinical and four private; and two of xanthoma tuberosum, one at the clinic and one in the office. I had the remarkable good fortune last year to have no less than six cases of xeroderma pigmentosum. Why do we not call it malignant progressive freckles? My first case of this disease I reported fourteen years ago in the *Journal of Cutaneous Diseases* in 1907, p. 473, and I have seen no more since that time until last year, when these six patients presented themselves. One was a private patient and I had him for a season in the hospital, treating his epitheliomatous growths. I hope to report his case at further length in the near future. The other five cases were clinical cases. One was a cretin, 29 years of age, with undeveloped genitals and of dwarfish stature. He declared his brother suffered from the same malady, but we have been unable to induce him to bring his brother to the clinic. The others were two brothers from the foot of Lebanon, and two sisters from a village some 1500 meters above the sea in northern Lebanon. The mother with her daughters traveled several days on foot to the hospital, dreading for the girls the cancerous fate that overtook their father. Six cases of this mysterious malady in one year I feel are more than my share!

ROENTGEN DERMATITIS AND RADIUM DERMATITIS: A COMPARISON

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It is not the purpose in this short article to discuss the detailed symptomatology of dermatitis caused by radium or that provoked by roentgen rays—the symptomatology of both is well known to practical workers in the field.

Some authors aver that in many respects there is a pronounced difference between injuries caused by radium and those caused by roentgen rays. It has been stated that radium dermatitis is less severe than roentgen dermatitis, that it heals more quickly and that it is not followed by sequelae, or that sequelae are less likely to occur. Also the fact that keratoses, subsequent to roentgen dermatitis, will yield to radium therapy much more readily than to roentgen therapy has been used as evidence in favor of a totally different action on the part of the two agents.

That there is some difference in the reaction and some difference in the action of the two agents cannot be denied, but such broad statements as those made in the foregoing are inaccurate and misleading. They give a false sense of security to the clinician who is entering the field of radium therapy.

A clinical and histopathologic study of radium dermatitis and roentgen dermatitis, together with a knowledge of the literature, necessitates the opinion that there is no essential difference between the reactions caused by the two agents.

There is, however, a difference in some details. Unfiltered radium ("soft" beta rays) will cause a reaction that is limited principally to the epidermis and papillary body. The erythema and edema may be intense and the epidermis totally destroyed. A reaction of this type, when viewed by one whose experience has been limited to roentgen dermatitis, causes profound perturbation. This is a second degree reaction, and if provoked by roentgen rays, several months would be required for complete healing, after which sequelae, such as atrophy, scarring, telangiectasia, keratoses, etc., would be likely to develop. A second degree reaction occasioned by "soft" beta rays heals quickly (in two or three weeks) and is much less likely to have sequelae. The rapidity of repair and completeness of repair is simply a question of the degree and depth of the injury. The injury to the epidermis is of no importance. If the derma has not been injured beyond repair, recovery will be rapid, complete and permanent.

This is the type of reaction provoked by the very "soft" beta rays. These rays, being extremely active ionizers, are rapid in action but they are mostly absorbed by the first few millimeters of tissue. The more penetrating beta rays reach and are absorbed by the deeper tissues, but the dose received by the deeper layers of the derma from the customary exposure with unfiltered applicators, is usually not sufficient to injure the true skin permanently.

The superficial character of reactions occasioned by very "soft" beta rays has been demonstrated not only by histopathologic investigation, but also by the fact that sequelae are uncommon and because not infrequently hair will continue to grow after second degree reactions.

It should be clearly appreciated, however, that if the penetration and the quantity of beta radiation is sufficient to injure the true skin seriously, as happens with lightly screened applicators, and at times with unscreened applicators, then the picture will be in all respects the same as that of roentgen dermatitis.

Experimentally it is possible to obtain superficial reactions with roentgen rays—2-inch spark gap with the glass wall of the tube in contact or very close to the skin—but we have never been able to duplicate with roentgen rays the extremely superficial effect obtained with very "soft" beta rays of radium.

Many clinicians, when desiring to utilize gamma rays, cover the applicator with lead, and then place the lead-covered applicator against the skin or mucosa. As is well known, the heavy elements, when acted on by roentgen rays, gamma rays and beta rays, emit a secondary radiation having definite characteristics. The secondary radiation from lead is very "soft" (slight penetration) and will effect the same type of reaction produced by very "soft" beta rays. It is this reaction that created the idea in the minds of some clinicians that there was a profound difference between the reactions effected by roentgen rays and those provoked by gamma rays of radium. All who have had experience know that "burns" from secondary radiation can be prevented by covering the lead with aluminum, glass, leather or any substance that gives rise to few or no secondary rays.

With the exceptions noted, it is our opinion that there is no material difference between the reactions occasioned by the two agents. Penetrating beta rays and gamma rays effect reactions that are histologically and clinically indistinguishable from roentgen-ray reactions. Unfiltered roentgen rays and lightly screened radium will destroy the skin, subcutaneous tissue and even the underlying muscles. Heavily filtered roentgen rays and radium, in sufficient quantity, will destroy or seriously injure tissue to a much greater depth than will lightly-

filtered radiation. This deep effect is also enhanced by distance from the source. Heavily filtered radiation applied from a distance may even cause necrosis of the subcutaneous tissues and muscles before the skin breaks down.

It will be seen from the foregoing that the detailed symptomatology depends on the conditions under which the exposure is made, but that fundamentally the reaction is the same whether produced by roentgen rays or radium. We have seen all the symptoms and all the sequelae that constitute acute, subacute and chronic roentgen dermatitis (including the so-called roentgen-ray skin) duplicated by radium.

The fact that keratoses, due to previous roentgenization, can be cured with radium more readily than with roentgen rays is not at all mysterious or confusing. Keratoses, regardless of etiology (roentgen rays, radium, sunlight, senility, etc.) are fundamentally the same. Keratoses that appear subsequent to excessive roentgenization develop years after the treatment, and they respond to the same treatment as do keratoses from other causes. The so-called roentgen-ray keratoses may be cured with properly applied roentgen-ray treatment or with adequate applications of gamma rays. We have noted no difference in efficacy in this respect between roentgen rays and gamma rays. Beta rays are the most efficacious of any type of radiation for this purpose, when properly applied. It is possible to obtain an intense beta ray effect to a depth of at least 1 cm., and this is all that is required in the treatment of keratoses. There is reason to believe that beta rays would be more efficacious than roentgen rays or gamma rays in epithelioma, if it were possible to obtain an intense effect to a depth of several centimeters without undue injury to the more superficial tissue. It is also possible that it is the secondary beta radiation evolved in tissue acted on by roentgen rays and gamma rays that produces the therapeutic result. If so, then the penetrating roentgen rays and gamma rays simply provide a source of beta radiation at various depths below the surface.

CONCLUSION

In conclusion, we repeat that there is no essential difference between the reaction provoked by radium and the reaction effected by roentgen rays. What little difference there is, is occasioned by the fact that very "soft" beta radiation produces a more superficial "burn" than do gamma rays or roentgen rays of long wave length, and that the shortest gamma rays effect much deeper destruction with correspondingly less superficial destruction than do the shortest roentgen rays, under the usual working conditions. It is becoming the practice in Germany to use a 12-inch to 14-inch spark gap and a skin-target distance of several

feet when employing roentgen rays in deep therapy. It is possible that radiation of this kind may destroy tissue to as great a depth as very short gamma rays, as the latter are used in practice at the present writing.

What we especially desire to emphasize is that no matter how radium is employed, if the quantity is sufficient, the results may be the same as those of the roentgen rays. We have seen atrophy and telangiectasia follow a single erythema dose administered with an unscreened, flat radium applicator of the varnished type.

REMEDIES FOR RHUS DERMATITIS

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Practical therapeutics may be deductive or inductive; may, that is to say, be based on some general principles which in their turn depend on the conceptions held as to disease processes and the pharmacodynamics of certain substances; or they may be merely the result of more or less discrete observations as to the curative value of such substances in certain diseased conditions. The former method in therapeutics is often spoken of as *rational,* and the latter as *empiric.*

EMPIRIC REMEDIES

In the list of remedies for rhus dermatitis of the empiric type, we may include all those remedies that do not take into account the chemical composition of the poison. Horsfield,[1] 1798, before anything regarding the chemical nature of the poison was known, listed these remedies: ashes of the leaves and wood of the poisonous rhus, soot dissolved in milk, an aqueous solution of sodium chlorid, copper sulphate, or ammonium chlorid, leaves of Datura stramonium, juice of Sanguinaria canadensis, unguentum simplex, sweet oil, and emollient cataplasms, and an ointment of 1 dram of saccharum saturni with 1 ounce of unguentum simplex. Christy[2] (1829) recommended topical applications of solutions of either lead acetate, ammonium chlorid or an infusion of digitalis. He advocated producing blisters above inflamed parts. He recommended solidago canadensis, an Indian remedy, and said its roots were chewed and part of the resultant saliva swallowed and part rubbed on the inflamed area. Dakin,[3] writing also in 1829, used locally in the treatment of this disease this prescription:

		gm. or c.c.	
R	Copper sulphate	4	℥ i
	Precipitate of red mercury	4	℥ i
	Venice turpentine	12	℥ iii
	Lard	30	℥ i

Mix to form an ointment.

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1. Horsfield, Thomas: An Experimental Dissertation on the Rhus Vernix, R. Radicans and R. Glabrum, Inaugural Dissertation for the Degree of M.D. at the University of Pennsylvania, 1798. Also in Medical Theses of University of Pennsylvania by Charles Caldwell **1**:117-163, 1805.

2. Christy, A.: An Essay on the Poisonous Qualities of Some Species of the Genius Rhus of Linneaus, New York Med. and Phys. J., N. S. **1**:21-30, 1829.

3. Dakin, R.: Remarks on the Cutaneous Affection Produced by Certain Poisonous Vegetables, Am. J. M. Sc. **4**:98-100, 1829.

In 1836, Pickett [4] records the local application of an old Massachusetts Indian remedy of an infusion of the bruised leaves and twigs of Diervilla canadensis (bush honeysuckle).

In 1837, an anonymous article [5] appeared, in which the treatment recommended for rhus poisoning included a topical application of from 20 to 40 grains of silver nitrate to 1 ounce of water, the skin having previously been washed clean with warm water and soap. A topical application of from 10 to 20 grains of mercuric chlorid to 1 ounce of water is not considered so good as the silver nitrate. Remedies which are considered as of little or no value, whether in weak or strong solution, are: Diervilla canadensis, Prot. lead acetate, potassium nitrate, potassium carbonate and sodium chlorid.

Smith,[6] in 1851, was led to use tincture of iodin in rhus poisoning, as it had been considered beneficial in the treatment of venomous reptile bites.

In 1858, Dr. Joseph Khittel [7] announced that the poison of rhus toxicodendron is a volatile alkaloid. Seven years later, in 1865, Maisch [8] in contrast to Khittel, considered the poison a volatile organic acid, which he named toxicodendric acid. These investigations had a noticeable effect on the rational treatment of the disease; but they are cited here merely to show that old remedies continued to be used and new ones were recommended, which did not take into consideration the volatile alkaloid of Khittel nor the volatile acid of Maisch.

In 1867, Canfield [9] described the mode of using Grindelia robusta and G. hirsutula as antidotes for poison oak. Either the bruised fresh herb was rubbed on the affected parts or a strong decoction, made by boiling either the fresh or dried herb, was used to wash the poisoned surfaces.

Risk [10] (1871) recommended the local application of a decoction of white oak. He also cites the alum solution of Hopkins, Dunn's decoction of cottonwood leaves for internal use, and the following formulas of Bailey:

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4. Pickett, N. B.: Diervilla Canadensis, Boston M. & S. J. **15**:380, 1836-1837.
5. Erythema Venenosa, Boston M. & S. J. **17**:347-350, 1837-1838.
6. Smith, T.: Observations on the Treatment of External Poisoning by Vegetable Substances, West. Lancet **12**:293-295, 1851.
7. Khittel, Joseph: Wittstein's Vierteljahresschrift f. praktische pharmacie. **7**:348, 1858.
8. Maisch, J. M.: On the Active Principle of Rhus Toxicodendron, Am. J. Pharm. **38**:4-12, 1865.
9. Canfield, C. A.: Grindelia as an Antidote to Poison Oak, Pacific M. & S. J. **9**:294-298, 1867.
10. Risk, J. B. A.: Poison Oak, Cincin. M. Repertory **4**:316-318, 1871.

		gm. or c.c.	
℞	Mercuric chlorid	2	ʒ ss
	Distilled water	90	ʒ iii
Add and dissolve			
	Ammonium chlorid	4	ʒ i
	Potassium nitrate	8	ʒ ii

Sig.: Apply thoroughly three times a day.

Dr. James C. White[11] sums up the empiric treatment of the inflammation up to 1873 thus:

A great many remedies have been recommended, in both medical and botanical books, for the treatment of persons poisoned by rhus, while others of a "domestic" character are used in various parts of the country. Among the former, a solution of acetate of lead holds the most conspicuous place. Torrey, in his "Botany of New York," says one of the best applications is a solution of sugar of lead, after the use of saline cathartics. Dr. Bigelow[12] thinks the application of acetate of lead as useful as any external palliative, and that it should be used as cold as possible. Solutions of sulphate of copper and of other metallic salts have also been recommended by physicians. Among the domestic remedies, vinegar, and solutions of saleratus and carbonate of soda, are widely and highly esteemed. A decoction of Virginia snakeroot (serpentaria) is also supposed to possess special power over the poison. In an old copy of Bigelow's "Florula Bostoniensis," picked up in a second-hand bookstore, I find, in connection with Rhus toxicodendron, a marginal note by its former owners, stating that, if soft-soap be rubbed thoroughly into the hands after handling specimens, its poisonous action will be prevented. The list comprises most of the other articles recommended by writers in medical journals as "cures" for rhus poisoning, many of which are stated to be "specific," and to act "like magic." It is needless to give the detailed directions for their application: Grindelia robusta, Comptonia asplenifolia, dulcamara berries (in cream), Cephalanthus occidentalis, Gelsemium sempervirens, rhamnus, Lactuca elongata, Collinsonia canadensis, Quercus alba (bark), Lindera benzoin, Sassafras officinale, Atropa belladonna, solutions of bromin, sulphate of zinc, chlorate of potash, chlorinated soda, sulphite of sodium, alum curd, and Turkish bath.

It is always a suspicious element in therapeutics when remedies are recommended as specifics, and when the list of cures for any one disease is exceptionally long. It is not strange, therefore, that we find even nonprofessional writers remarking that "the reputed remedies are more numerous than efficacious (Torrey and Gray)."

De Witt,[13] 1874, used the following prescription locally:

		gm. or c.c.	
℞	Glycerin	60	gr. x
	Tinct. iodin	15	ʒ ii
	Carbolic acid	2	ʒ ss
	Morphin sulphate	0.66	ʒ ss

11. White, J. C.: On the Action of Rhus Venenata and Rhus Toxicodendron on the Human Skin, New York M. J. **17**:225-249, 1873.

12. Bigelow, J.: Am. Medical Botany **1**:96; **3**:20, 1817-1820.

13. De Witt, W. H.: Poisoning by Rhus Toxicodendron, Am. J. M. Sc. N. S. **67**:116-118, 1874.

Humphrey [14] in the same year recommended sponging the surface every hour with one part of zinc sulphate in twenty-four parts of water.

Morrison,[15] 1874, published the following formula to be applied constantly to the affected parts:

		gm. or c.c.	
℞	Carbolic acid	2	f℥ ss
	Sodium sulphite	12	ʒ iii
	Water	120	f℥ vi

He said that he did not know that the sodium sulphite was of any use in the formula; but he knew that it would not be of much use without the phenol (carbolic acid).

An anonymous contributor [16] printed, in 1875, a prescription of mercuric chlorid, 10 grains, and lime water, 5 ounces, to be used locally. This he preferred to: sodium chlorid and potassium bicarbonate, lead acetate, lead paint thinned with linseed oil, gunpowder and water, ammonia water and olive oil.

In 1876, Yandell [17] recommended a dram of quinin in twelve pills, one-third to be taken each afternoon, with no local treatment. Of external applications, he considered mercuric chlorid the best.

In 1876, Bernard [18] used the fluid extract of Gelseminum sempervirens, externally, with good results.

Brown,[19] in 1878, stated that bromin was a cure for rhus poisoning when applied externally as a mixture of from 10 to 20 drops of bromin to an ounce of olive oil, petrolatum or glycerin. This was to be rubbed gently on the affected parts, three or four times a day, and especially on going to bed at night. The oil was washed off twice daily with castile soap.

The year 1879 was a popular year for rhus remedies; at least seven were published. Those authors that did not state the chemical nature of the poison were Kahler,[20] Osborn [21] and Smythe.[22] Kahler used for

14. Humphrey, C. H.: Sulphate of Zinc in the Treatment of Poisoning by Rhus Radicans, Am. J. M. Sc. **68**:160, 1874.

15. Morrison, S. W.: Poisoning by Rhus Radicans, Phila. M. Times **5**:629, 1874-1875.

16. Poisoning by Rhus Toxicodendron, Med. and Surg. Reporter **33**:306, 1875.

17. Yandell, L. P.: Poison Oak Eruption, Louisville Med. News **2**:32, 1876.

18. Bernard, E. H.: Poison Oak Eruption, Louisville Med. News **2**:91, 1876. Sumach, Med. Rec. **13**:320, 1878.

19. Brown, S. A.: A Remedy for the Eruption of Poison Oak, Ivy and Sumach, Med. Rec. **13**:320, 1878.

20. Kahler, R.: Poisoning by Rhus (Tinct. Lobelia an Antidote), Med. Brief **7**:22, 1879.

21. Osborn, T. C.: On Poison Vine Eruption, Am. M. Bi-Weekly **10**:49-50, 1879.

22. Smythe, A. G.: Rhus Poisoning, Med. Rec. **16**:284, 1879; Arch. Dermat. **4**:320, 1879.

local application a mixture of ammonia water, 1 dram and tincture of lobelia, 7 drams, every two or three hours. Osborn used locally a cloth saturated with lime water overnight, to be exchanged the next morning for a bandage saturated with oak bark decoction. Smythe applied to the affected parts soft cloths, kept wet with a saturated solution of sodium thiosulphate.

Within the decade between 1880 and 1890, published remedies and "specifics" became more numerous. Blackwood [23] (1880) secured no real benefit by the use of alkalies (ammonia, sodium and potassium), the sulphites and bisulphites, solutions of bromin, iodin, phenol, potassium permanganate, saturated infusions and tinctures of serpentaria and lobelia, stale beer and milk. The use of lime water he considered the best local treatment. Burgess [24] (1880) recommended the local application of a solution of lead acetate (2 drams to a pint of water) on lint covered with oiled silk. Hardaway,[25] in 1881, specified a formula of ½ ounce of zinc sulphate in one pint of water for local use. In 1882, Edson,[26] having used gelsemium for some years with much satisfaction in pruritic troubles, believed that it might at least alleviate the pain in rhus dermatitis. He used the following formula which speedily stopped the pain:

		gm. or c.c.	
℞	Phenol	2|	ʒ ss
	Fluidextract of gelsemium	8|	ʒ ii
	Glycerin	16|	ʒ ss
	Water, sufficient to make	120|	ʒ iv

Kunze [27] (1883) recommended local treatment with lactic acid, acetic acid or salt water and lime juice. The lactic acid idea was the result of the buttermilk remedy, the acetic acid came from Central and South America and salt water and lime juice are popular remedies for manchineel poisoning. Hinton [28] (1883) stated recovery follows within twenty-four hours if a strong infusion of red sassafras root is applied frequency. Leonard [29] (1884) gave the following list of four topical remedies:

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23. Blackwood, W. R. D.: Some Thoughts on Rhus Poisoning, Phila. Med. Times **10**:618-619, 1880.
24. Burgess, T. J. W.: On the Beneficent and Toxical Effects of the Various Species of Rhus, Canad. J. M. Sc. **5**:327-334, 1880.
25. Hardaway, W. A.: Rhus Poisoning, St. Louis Cour. Med. **6**:401-402, 1881.
26. Edson, B.: Gelsemium in Rhus Poisoning, Med. Rec. **22**:121-122, 1882.
27. Kunze, R. E.: Poison Rhus, Med. Tribune **5**:111-120, 1883.
28. Hinton: Sassafras in Rhus Poisoning, Chicago Med. Rev. **7**:15, 1883.
29. Leonard, W. W.: Rhus Poisoning, Med. Chron. **3**:21-22, 1884-1885.

		gm. or c.c.	
℞	Tinct. lobelia	60	ʒ ii
	Sodium bicarbonate	4	ʒ i
	Water	60	ʒ ii
℞	Sodium thiosulphate	30	ʒ i
	Water	500	O i
℞	Spirit of nitrous ether applied without dilution several times a day.		
℞	Bromin	2–4	ʒ i
	Olive oil	30	ʒ i

Tate [30] (1885) recommended the application of copper sulphate, 2 drams in water, 8 ounces, to stop the pain and burning.

At least seven remedies were published by different authors in 1886. Of these, an anonymous author [31] recommended an infusion of sweet fern (Comtonia asplenifolia) to be applied locally. Barnes [32] recommended this compound to be taken internally:

		gm. or c.c.	
℞	Sodium phenol sulphonate	6	ʒ iss
	Fluidextract of gelsemium	4	ʒ i
	Water, sufficient to make	120	fʒ iv

Sig.: One teaspoonful every two hours.

Brown [33] published this modification of his 1878 remedy:

		gm. or c.c.	
℞	Bromin		♏ x-xx
	Olive oil or oil of sweet almond	30	fʒ i

L. D. M.[33a] gave as a remedy the following:

℞	Pulverized borax	ʒ ii
	Phenol	ʒ i
	Morphin sulphate	gr. x
	Compound powder of acacia	ʒ iv
	Water, sufficient to make	ʒ viii

In criticism of this mixture, he stated that phenol and borax "help to kill the poison," and the gum acacia helps to allay irritation and pruritus. Regensburger [34] recommended Russian baths in the treatment of Rhus diversiloba dermatitis.

In 1887, Baldwin [35] announced a remedy in phenol ointment U. S. P., and recommended as local California remedies an infusion of Grindelia robusta, bay berry bush, eucalyptus, and buckeye. Couch [36] in the same

30. Tate, W. H.: Cutaneous Poisoning with Rhus Toxicodendron, Peoria M. Month. **6**:198, 1885-1886.

31. Jour. Cután. and Vener. Dis. **4**:160, 1886.

32. Barnes, Edwin: Med. Rec. 1886, pp. 157-158.

33. Brown, A.: Med. and Surg. Reporter **54**:762, 1886.

33a Rhus Diversiloba Remedy, Med. and Surg. Reporter **54**:603, 1886.

34. Regensburger, A. E.: Treatment of Rhus Poisoning, J. Cutan. and Vener. Dis. **4**:244. 1886.

35. Baldwin, A. E.: A Case of Poisoning by Rhus Toxicodendron, Pacific M. & S. J. **30**:509-512, 1887.

36. Couch, L. B.: The Treatment of Rhus Poisoning, Med. Rec. **32**:486, 1887.

year recommended frequent and thorough washing with hot soapsuds, and asserted that this treatment removed the irritant.

Hawley,[37] in 1890, stated that the use of oil of palustre ledum 3x if administered when the eruption first appeared would cause all symptoms to disappear within forty-eight hours.

Aulde [38] used whitewash externally in 1890. Kite [39] used black mercurial lotion similarly in 1891. Other external applications recommended in 1891 were a decoction of chestnut leaves (Castanea fagus) by Straley,[40] thymol iodid by Levick,[41] concoction of fluid extract of serpentaria (Virginia snakeroot) Walker.[42]

In 1894, Cantrell [43] used full strength solution of chlorinated soda (Labarraque's solution) with good results in seven cases.

An anonymous author,[44] in 1895, recommended the juice or infusion of the touch-me-not (Impatiens fulva). Cantrell [45] recommended phenyl salicylate (salol) and Labarraque's solution. Witmer [46] in the same year published, as a topical application, lead water and opium, to be used during the acute stage with ½ grain of mercuric chlorid internally, every three hours.

Brown [47] two years later (1897), considered a mixture of equal parts of lime water and linseed oil a good external application; and Clarke [48] recommended a solution of borax. During the same year Smith [49] recommended lime water as effective; Todd [50] prescribed black mercurial lotion; Gilpin, fluid extract of serpentaria; Cloyd [51] the juice of the wild touch-me-not; Winfield,[52] a paste of 0.5 to 1 per cent.

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37. Hawley, J. W.: Rhus Poisoning, Med. Advance **24**:257-262, 1890.
38. Aulde, John: Med. and Surg. Reporter **63**:360-365, 1890.
39. Kite, J. A.: Weekly Med. Review **23**:12, 1891.
40. Straley, S. B.: Weekly M. Review **23**:166, 1891.
41. Levick, J. J.: Med. News **59**:105, 1891.
42. Walker, J. B.: Poisoning by Ivy at Second Hand, Med. News **59**:556, 1891.
43. Cantrell, J. A.: A Treatment for Ivy Poisoning, Phila. Polyclinic **3**: 181-182, 1894.
44. An Antidote for Poison Ivy, Kansas M. J. **7**:633, 1895.
45. Cantrell, J. A.: Phila. Polyclin. **4**:99, 450, 1895.
46. Witmer, A. F.: Mercuric Chlorid in the Treatment of Rhus Poisoning, Phila. Polyclin. **4**:267, 1895.
47. Brown, C. A.: Poisoning by Rhus Toxicodendron, Med. Brief **25**:704, 1897.
48. Clarke, T. H.: Rhus Toxicodendron Poisoning, Med. Brief **25**:1006, 1897.
49. Smith, C. D.: Med. Brief **25**:1195, 1897.
50. Todd, J. D.: Rhus Toxicodendron Poisoning, Med. Brief **25**:696, 1897.
51. Cloyd, A. D.: Med. Brief **25**:916, 1897.
52. Winfield, J. M.: Brooklyn M. J. **11**:404, 1897.

ichthyol, with magnesium carbonate, olive oil and simple ointment; Bartley,[53] sodium bicarbonate or lye water; and Hunt,[54] red mercuric iodid.

Next year (1898), Frank [55] prescribed baths followed by antiseptic emulsions containing calamin, glycerin, lime-water and the like.

In 1903, Klotz [56] used one part icthyol to three parts of water as an application for the inflamed area; Thudichum,[57] three drops of tincture of rhus to two-thirds glass of water, a teaspoonful of the mixture to be taken three times daily, and boric acid to be used as a dusting powder. Thudichum said his daughter, having used lemon juice to remove freckles, tried it for poison ivy, and a cure resulted within thirty-six hours. Pollard [58] used a decoction of California "buckbrush" leaves locally. Hughston [59] (1905) applied with unvarying success lead acetate 10 grains, mixed with spirit of nitrous ether, 1 ounce.

In 1906, Daniel [60] considered a mixture of quinin sulphate in water a *specific,* and it cured more rapidly than calomel, 16 grains mixed with 4 ounces of lime water. Milton [61] believed immunity to rhus poisoning resulted from a few doses of European anacardium.

Lindley,[62] in 1908, recommended a solution of lead acetate and tincture of deodorized opium preferable to alcohol, hydrogen peroxid, boric acid and potassium permanganate. An anonymous writer [63] used a calamin and lead lotion.

Ellis [64] (1910) considered the best remedy sodium bicarbonate, when used as a dusting powder and covered with lime liniment. This he believed to be better than a saturated solution of sodium thiosulphate, a saturated solution of borax, a lead and opium wash, talcum powder, phenol ointment (1-30), iodin ointment, camphorated phenol ointment, lead acetate solution, zinc sulphate solution, and thymol iodid.

RATIONAL REMEDIES

Rational topical remedies are considered as based on general therapeutic principles and more or less erroneous conceptions of the chemical

53. Bartley, E. H.: Brooklyn M. J. **11**:405, 1897.
54. Hunt, J. H.: Rhus Poisoning, Brooklyn M. J. **11**:392-406, 1897.
55. Frank, L. F.: Med. Rec. **53**:551-554, 1898.
56. Klotz, H. G.: Merck's Arch. **5**:225, 1903.
57. Thudichum, C. L.: Rhus, Skookum Chuck, Alkaloidal Clinic **10**:831-834, 1903.
58. Pollard, F.: Poison Oak, Alkaloidal Clinic **10**:599, 1903.
59. Hughston, W. L.: Poison Ivy, Med. Brief **33**:678-679, 1905.
60. Daniel, T. J.: A Specific for Rhus Poisoning, Med. World **24**:299, 1806.
61. Milton, R. L.: Med. World **24**:59-60, 1906.
62. Lindley, J. S.: Rhus Poisoning, Am. J. Dermat. **12**:342-344, 1908.
63. British M. J. **11**:545, 1910.
64. Ellis, Richard: Poison Ivy Rash, Med. Rec. **78**:160-161, 1910.

nature of the poison and its pharmacologic action. The list of these remedies seems to begin with Horsfield [1] in 1798. Owing to the incomplete chemical analyses of Khittel,[7] in 1857, and Maisch,[8] in 1865, by which the poison was first considered a volatile alkaloid and then a volatile organic acid, more remedies were produced. Burrill,[65] in 1882, believed the disease to be caused by a specific parasite that infests the rhus (a view supported by Hubbard [66] in 1885, and Frost,[67] in 1916), and introduced disinfectants among the list. The work of Pfaff,[68] in 1897, which resulted in the poison's being considered a nonvolatile oil, was the cause of still other remedies. Acree and Syme [69] by their discovery, in 1906, of a supposed toxic glucosid of fisetin, rhamnose and gallic acid in R. toxicodendron made further alterations in the list necessary. Despite the successive discoveries as to the nature and cause of rhus dermatitis, the list of remedies, instead of decreasing, increased with each successive experiment. There were physicians who until 1908 (two years after the work of Acree and Syme) still believed the active principle to be the toxicodendric acid of Maisch and others who insisted upon its being the toxicodendrol of Pfaff.

If those substances and methods which have been used to allay the pain, itching and systemic effects, as well as those that assist involution, are excluded the list of remedies is not nearly so long as those of the empiric or inductive type.

The first substance used in an attempt at rational treatment was mercuric chlorid. This was employed by Horsfield (1798) with the hope that by its corrosive action on the skin the poison would be thrown off the affected area.

The next attempt at rational treatment involved the employment of those chemicals which when added to the poison in laboratory glassware might be expected to produce nontoxic compounds. To my present knowledge, the first experimenter in this line was Maisch (1865). In this connection he says:

> As remedies against it, I have tried subacetate of lead, permanganate of potassa and ammonia, the last, I believe, with the best success. Alkaline solutions were first recommended by Professor Procter, I believe, and, as my experi-

65. Burrill, T. J.: Some Vegetable Poisons, Am. Monthly Microscop. J. **3**: 192-196, 1882.

66. Hubbard, S.: Rhus Toxicodendron, Peoria Med. Monthly **6**:323-324. 1885-1886.

67. Frost, L. C.: Bacterial Etiology of Poison Oak Dermatitis (Rhus Poisoning), Med. Rec. **90**:1121-1123, 1916.

68. Pfaff, Franz: On the Active Principle of Rhus Toxicodendron, J. Exper. Med. **2**:181-196, 1897.

69. Acree, S. F., and Syme, W. A.: Some Constituents of the Poison Ivy Plant, Am. Chem. J. **36**:301-321, 1906.

ments show, they are the remedies which a priori might be expected to afford the greatest relief, just as in the case of formic acid. The eruption produced by this acid is very similar in its nature to the one produced by toxicodendric acid, and its effects yield readily to alkaline lotions. It is not unlikely that, like the formates, the toxicodendrates are without any ill effects, if applied externally. The reactions of our new acid show, likewise, the reason why permanganate of potassa, subacetate and even acetate of lead may be valuable remedies for this eruption. While the former completely decomposes it, the last named salts produce nearly insoluble precipitates with it; at least, toxicodendric appears to be stronger in its affinities than acetic acid.

Dr. James White,[11] writing in 1873 and again in 1887, considered the poison to be the toxicodendric acid of Maisch. With this idea in mind, he says:

We have to deal with an acid, and the antidote for an acid is an alkali, that is, provided the salts thus formed are not equally poisonous. In poisoning by oxalic acid, for instance, potash is not an antidote, because the combination formed is nearly as poisonous as the acid itself. Whether the salts formed with toxicodendric acid by ammonia, potash, and soda are likewise poisonous, Professor Maisch leaves us somewhat in doubt as the result of experiment, but speaking clinically he leads us to believe that they are not; for he says that the application of solutions of ammonia seemed to be most effective in counteracting the action of the acid. This is consistent with the popular reputation of solutions of saleratus and soda as remedies, and will explain the action of the soft-soap. These are true antidotes, but they can be of benefit only from their chemical action, and in this way.

Of the other writers who believed the poison to be the volatile toxicodendric acid of Maisch, Park,[70] in 1879, recommended the use of a camphor-chloral mixture (equal parts of each allowed to stand in the open air and liquefy); Brandt,[71] in the same year, used a saturated solution of sodium thiosulphate, externally and internally, and aborted the worst cases in from twenty-four to forty-eight hours. He also used alkaline bicarbonates and lime water locally and internally with "fair success," Ward[72] (1879) prescribed Labarraque's solution, concentrated when the skin was unbroken and diluted with from three to six parts of water when the skin surface was broken. Johnson[73] (1886) used externally a formula of sodium thiosulphate, 1 ounce, distilled water 8 ounces, phenol, 1.5 drams, glycerin, ½ ounce. Internally he used potassium iodid, 2 drams, distilled water, 7 ounces, syrup, 1 ounce, a tablespoonful four times a day. Beringer[74] (1896) used granular

70. Park, R.: Dermatitis Venenata—or Rhus Toxicodendron and Its Action, Arch. Dermat. **5**:227-234, 1879.

71. Brandt, W. E.: Poisoning by Rhus Radicans, Med. Rec. **16**:46-47, 1879.

72. Ward, J. M.: Poisoning by Rhus Radicans, Med. Rec. **16**:117, 1879.

73. Johnson, J. B.: Med. and Surg. Reporter **54**:508, 1886.

74. Beringer, G. M.: Rhus Poisoning, Am. J. Pharm. **68**:18-20, 1896.

sodium thiosulphate 1 dram, glycerin, ½ fluidounce, camphor water, sufficient to make 4 fluidounces; also he used hot soda baths, and as a preventive treatment washing the face and hands with a solution of hydrogen peroxid. Davis [75] (1897) considered as a remedy a warm bath for from 15 to 20 minutes at blood heat to which 4 ounces of borax had been added. The cuticle was dried and cosmolin applied. In one hour a strong solution of lead acetate, a weak ammonia water, sodium carbonate, alum curd, or a tincture of Grindelia squarrosa (?) was applied. Hadden [76] prescribed, in 1906, Labarraque's solution as better than alcoholic lead acetate; Conner [77] (1907) used sodium thiosulphate mixed with glycerin and phenol, or a solution of benzoic acid and solution of formaldehyd with an equal amount of saturated solution of sodium thiosulphate. He considered quinin solution of little value; and Ward [78] (1908) used as a lotion a saturated solution of aluminum acetate, or if this is not to be had, he used phenol from 2 to 4 per cent., sodium bicarbonate, sodium sulphite, lead acetate, lotion of lead and opium or black mercurial lotion.

When the poison was found to be a nonvolatile oil by Pfaff (1897), a modified method of treatment was prescribed. He recommended the precipitation of the poison with lead acetate, copper or iron. Ordinary oxidation, he says, is very slow, but may be slightly accelerated by a solution of sodium carbonate. He does not recommend the use of oxidizers, however.

Of the physicians who followed the discovery of Pfaff, Schwalbe,[79] in 1903, recommended the use of alkalies to destroy (saponify?) the oil; he accordingly prescribed a 0.1 to 0.5 per cent. solution of potassium carbonate or a 1 to 1.5 per cent. solution of ammonium chlorid. McKee [80] (1906) believed a formula consisting of alcohol 53 per cent., distilled water, 47 per cent., and lead acetate, sufficient to make a saturated solution, would give relief for from six to eight hours. Guernsey [81] (1913) considered a saturated solution of magnesium sulphate best, although he also recommended the use of strong soap and water to "neutralize the acidity of the oil," a 50 per cent. alcohol solu-

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75. Davis, W. T.: Rhus Toxicodendron Poisoning, Med. Brief **25**:938-940, 1897.

76. Hadden, A.: Poison Ivy or Rhus Toxicodendron, Med. Rev. of Rev. **12**:764-765, 1906.

77. Conner, J. J.: Poisoning by Rhus Toxicodendron, Am. J. Dermatology **11**:368, 1907.

78. Ward, R. F.: Severe Ivy Poisoning, New York M. J. **88**:1224-1225, 1908.

79. Schwalbe, C.: On the Active Principle of Rhus Diversiloba (Poison Oak), Med. Rec. **63**:855-856, 1903.

80. McKee, E. S.: Poisoning by Rhus Toxicodendron or Rhus Radicans, Med. Herald, N. S. **25**:98-100, 1906.

81. Guernsey, J. C.: Rhus Poisoning, Hahneman. Month. **48**:161-174, 1913.

tion of lead acetate, from 2 to 4 per cent. potassium permanganate, 1.5 per cent. ammonium chlorid, hydrogen peroxid, 1 teaspoonful of sodium carbonate to a quart of water, sodium thiosulphate, 1 part of household ammonia to 2 parts of water, a solution of alum, and thymol iodid or alum dusting powder.

Syme (1906) considered the poison a glucosid of rhamnose, fisetin and gallic acid. In counterdistinction to Pfaff, he recommended the use of an oxidizer, namely potassium permanganate. Syme said in part:

> The best example of the latter was obtained with the ether solution from the extraction of the lead precipitate in the Soxhlet apparatus. After removing the ether, a small drop of the residue was applied to the wrist as described. An itching red spot about the size of a dime was noticed in thirty-six hours, and it steadily increased in size. Nearly two days after the application of the poison, a dilute solution of potassium permanganate containing a little caustic potash was rubbed into the spot until the pimples were destroyed. A little black spot was left wherever there had been a pimple, showing that the permanganate had been reduced to oxid in the skin. The place was washed and nothing more was thought of it until the morning following, when it was noticed that the wrist had commenced to swell during the night, and the characteristic watery secretion was running from the poisoned spot. More permanganate solution was applied without potash and the wrist was bandaged, thinking that this would prevent the spreading of the eruption, but it really facilitated spreading by becoming saturated with the poisonous fluid and keeping it in contact with a larger surface of skin. In the meantime the swelling and inflammation had extended nearly to the elbow. The arm now had the appearance of having been bitten by a snake. To reduce the swelling it was immersed in hot water. This seemed to bring out the eruption very quickly and the blisters were treated with permanganate as fast as they appeared. The swelling was reduced, but returned during the night. On the evening following, the forearm was immersed in a bowl of hot permanganate solution containing a little caustic potash. The solution was kept as hot as could be borne for about half an hour. After this bath, the poison was completely oxidized, for the swelling was reduced and did not return, nor was there any fresh eruption. What appeared to be a severe case of poisoning was thus cured very quickly. The use of hot water not only reduces the swelling, but also helps to destroy the poison. The action of permanganate is also more rapid at high temperatures.
>
> The oxidizing power of permanganate, as is well known, is greater in acid solution than in alkaline, five atoms of oxygen being available in the former and three in the latter, according to these equations:
>
> $$2\ KMnO_4 + 3\ H_2SO_4 = K_2SO_4 + 2\ MnSO_4 + 3\ H_2O + 5O.$$
> $$2\ KMnO_4 + H_2O = 2\ MnO_2 + 2\ KOH + 3O.$$

Permanganate was used as a remedy in some cases mixed with dilute sulphuric acid, and in others, with zinc sulphate; also with lime water. It was found to be satisfactory whether used alone or with any of the substances mentioned, provided it was well rubbed into the skin. The concentration of the solution used was varied according to the location and condition of the eruption. Where the skin was thin or already broken, dilute solutions (1 per cent.) were used. In one case, the eruption appeared in the palm of the hand

where the skin was so thick that it was necessary to open it before the remedies could reach the poison. The difficulty of getting the remedy in contact with the poison in the skin is the reason why the eruption is hard to cure.

Syme also opposed the use of an alcoholic solution of lead acetate as a remedy:

This remedy is unsatisfactory for the reason that its action consists in depositing an unstable lead compound of the poison in the skin where the conditions of moisture and temperature are favorable for its decomposition, liberating the poison with all its irritant properties. Moreover, alcoholic preparations should not be used because the alcohol dissolves the poison and, on evaporation, lets it spread over a larger surface like a varnish. Potassium permanganate, however, oxidizes the poison completely. The only objection to the use of permanganate of which the writer is aware is that it stains the skin. The stain can be removed by vigorous scrubbing with soap, or it will wear off gradually in a few days. It can be removed at once by certain acids, but these should not be used by persons not familiar with their action.

Dr. Baird [82] on the strength of this knowledge recommended a 2 to 4 per cent. solution of permanganate in 1909.

According to my present knowledge, the next person who attempted to find an antidote through a search for a chemical neutralizer was Dr. von Adelung,[83] in 1912. He believed the poison to be the glucoside of Acree and Syme. His experiments in that line were as follows:

Experiment 14.—Ammonia water.—Equal parts of ammonia and tincture of rhus were mixed and tested on the skin. The mixture is toxic, from which it is evident that ammonia does not destroy the poison.

Experiment 15.—Peroxid of hydrogen.—Because it is a strong oxidizer, it was presumed that hydrogen peroxid would have some curative property. But when tested by adding it in equal quantity to the rhus tincture, it failed to inhibit the toxicity, and when tested, with control, on a patch of dermatitis it was found inert.

Experiment 16.—(Aristol.)—The left of two artificial patches of dermatitis was treated during five days with a solution of aristol in cotton-seed oil. The control received no treatment. Both were scratched. Result: The untreated patch recovered first.

Experiment 17.—The same test was made on the left of two spots produced by green leaves. The aristol in oil was applied five times in four days and protected by gauze held in place by plaster. Result: No difference could be noted. Aristol therefore appears to be of no value.

Experiment 18.—(Castor Oil.)—A mixture of equal parts of 10 per cent. tincture of rhus and castor oil was rubbed on the arm. In thirty-six hours there was a slight itching, but no eruption.

Experiment 19.—(Cedar Oil.)—A similar mixture with cedar oil was applied to the arm. After thirty-six hours, a slight eruption appeared which later developed into a fair patch of itching dermatitis.

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82. Baird, A. W.: Ivy Poisoning, Med. Rec. **76**:232, 1909.

83. Von Adelung, Edward: An Experimental Study of Poison Oak, Arch. Int. Med. **11**:148-164, 1913.

Experiment 20.—(Cottonseed Oil.)—A similar mixture with cottonseed oil was applied to the thin skin of the wrist. After eight days no dermatitis had appeared.

Experiment 21.—Cottonseed oil in which green leaves had been soaked for twenty-four hours was applied to the arm. The result was slight dermatitis. This, repeated on another person, gave the same result.

Experiment 22.—Some cottonseed oil in which green leaves had been heated was applied to the arm. After four days, itching began, and in five days, a slight eruption.

Experiment 23.—A mixture of equal parts of tincture of rhus and cottonseed oil was applied to the arm. No dermatitis was detected in eight days.

These results raised the question whether cottonseed oil did not combine chemically with the toxin, destroying the toxicity. To test this point, the mixture of oil and tincture was allowed to stand a few days, when the tincture formed a layer above the oil. This supernatant fluid was toxic, producing dermatitis.

Experiment 24.—A mixture of equal parts of tincture rhus and of tincture of green soap was applied to the arm and protected by gauze. After twenty-four hours only a slight eruption was noted.

Experiment 25.—A mixture of tincture of rhus, 25 parts, and tincture of green soap, 5 parts was applied to arm and protected with gauze. Only slight dermatitis resulted.

Experiment 26.—After allowing tincture of green soap to dry on a spot, tincture of rhus was applied. A control spot was made with the rhus alone. Both spots were protected with gauze. The control took well, while the soaped spot showed a slight dermatitis. Thus it appears that soap deters the poison of rhus.

Experiment 27.—(Ichthyol Collodion.)—The worse of two patches of dermatitis, three days old, was painted with a 5 per cent. ichthyol collodion daily. In twenty-four hours, distinct improvement was noted in the treated patch, and this patch recovered earlier. This was confirmed in treating hospital cases.

Experiment 28.—(Hyposulphite of Sodium.)—Tests with this substance were also negative. It failed to inhibit the toxicity when added in large proportion to the tincture of rhus; and it failed to show curative effect on dermatitis patches compared with controls.

Experiment 29.—(Iodid of Potassium.)—This substance in strong solution, added to an equal part of tincture rhus, failed to inhibit the toxicity as tested on the skin.

Experiment 30.—(Tincture of Iodin.)—Full official strength tincture of iodin when mixed with an equal quantity of tincture of rhus destroys the poison; for when this mixture is tested on my arm no dermatitis results. If, however, the strength is reduced to less than 5 per cent. of the mixture, by addition of water or alcohol, the toxicity is not destroyed completely.

Experiment 31.—Tincture of iodin also has curative property. To one of two patches of dermatitis, official tincture of iodin was applied. The application burned. But the treated patch recovered earlier than the control. Itching quickly subsided and healing followed. The spot remained discolored and tender, presumably from iodin burning.

Experiment 32.—The right of two patches of dermatitis was rubbed with 90 drops of water mixed with 10 drops of tincture of iodin. The control was rubbed with alcohol. The application of iodin caused a burning sensation, not

severe. In twenty-four hours the rhus dermatitis had disappeared, but was replaced by an iodin burn. The control ran a normal course.

Experiment 33.—(Potassium Permanganate.)—A mixture of equal parts of potassium permanganate (0.56 gm. in 120 c.c.) with tincture rhus, when tested on the arm was found to be absolutely nontoxic.

Experiment 34.—One of two patches of dermatitis was painted with potassium permanganate in the above strength. The treated patch healed earlier than the control.

Experiment 35.—(Magnesium Sulphate.)—Chemical Tests: A fresh rhus leaf macerated with a saturated solution of magnesium sulphate remained toxic, as proven by testing on my arm.

Experiment 36.—Saturated solution of magnesium sulphate (Squibb's), added in equal quantity to tincture rhus, does not inhibit the toxicity, for dermatitis results when the mixture is applied to the skin.

Making use of the solubility of rhus poison, therapeutic experiments have been based on the remedial value of solvents as well as chemical agents. Maisch and White considered the poison soluble in water and recommended that parts exposed to rhus be immediately washed or bathed for a considerable time in water. Pfaff prescribed the mechanical removal of the poison as soon as possible after exposure by vigorously washing the affected and exposed parts with soap, water and a scrubbing brush. As the poison is soluble in alcohol, Pfaff likewise believed in thoroughly washing with alcohol and a scrubbing brush, or in washing the exposed parts with an alcoholic solution of lead acetate. He also recommended the use of oils, including petrolatum, if quickly removed and repeatedly used so as not to spread the poison. Syme, as previously quoted, believed the poison would be spread by the use of alcoholic lead acetate. Stevens [84] (1906) obtained the best results by rubbing the surface with a little petrolatum, which he scraped off with a knife, and washing the surface with a weak solution of sodium hydroxid or carbonate. He also, recommended alcohol, petroleum benzin, ether or kerosene as washes to remove the poison. As heretofore quoted, von Adelung experimented with castor, cedar and cottonseed oils.

In the belief that the poison was Pfaff's toxicodendrol, Balch [85] (1906) said:

> The use of soap and water and a good hand brush is the simplest method of getting rid of the oil. The action is entirely mechanical and is perfectly efficient. Alcohol dissolves and removes the oil, but successive portions must be allowed to flow over the part as after contact the alcohol may contain sufficient oil to spread the irritation. Ordinary alcohol must be used and not 50 per cent. alcohol as the latter does not dissolve the oil. The action is purely a solvent one and not one of neutralization.

84. Stevens, A. B.: Japanese Lac, Inaugural Dissertation, Ann Arbor, Mich., 1906.

85. Balch, A. W.: Poison Ivy, J. A. M. A. **46**:819-820, 1906.

Guernsey (1913), also a follower of Pfaff, recommended the use of a wash of alcohol, whisky or ether to remove the poison.

Many physicians have made clinical comparisons of various popular remedies, with or without taking into consideration the chemistry of the poison. Such comparisons of remedies, which were made successively on the same patient and therefore in different stages of the disease, are considered untrustworthy and are therefore eliminated. The earliest of these comparisons is that of Dr. Bigelow [12] (1820). He says:

> The acetate of lead is perhaps as useful as any external palliative, and it should be used in solution rather than in the ointment, that it may be applied as cold as possible. The late Dr. Barton speaks highly of a solution of corrosive sublimate externally applied in this disease, but from trials of the two remedies made at the same time and in the same patient, I have found the lead the more beneficial of the two.

Cantrell [86] (1898), who carried his experiments over a long period of time and who had an abundant opportunity for experimental work, summed up the relative values of certain drugs in the treatment of ivy poisoning in order of preference, as follows: First, Labarraque's solution (dilute in erythematous and concentrated in vesicular); second, phenyl salicylate (salol) 0.5 dram to the ounce of petrolatum liquefied or ether, because both produce a cure in less than a week's time; third, bromin (10 grains to the ounce of some oily substance) cures in about ten days; fourth, boric acid (saturated or dilute solution) cures in about two weeks; fifth, acetanilid (½ dram to 1 dram to the ounce of liquid petrolatum) cures in about two or three weeks, because they may be relied on to produce no ill effects; sixth, *Grindelia robusta* (fluid extract 2 drams to the pint of water, more concentrated irritates), cures in about two weeks. This can always be relied on to produce a cure, but it is long delayed and may if not watched carefully produce a higher grade of inflammation.

Von Adelung in 1912 carried on comparative therapeutic tests as follows:

> Though magnesium sulphate fails to destroy the toxicity of rhus when mixed with its tincture, or its juice, it, nevertheless, possesses definite therapeutic value.
>
> Experiment 37.—Test 1: In one of two patches of dermatitis, saturated solution of magnesium sulphate was rubbed three times at hour intervals. By the next morning the treated patch was better than the control. Three more similar applications were made during the forenoon and by noon a very marked improvement was noted. The treated patch recovered earlier than the control.

86. Cantrell, J. A.: Relative Value of Certain Drugs in the Treatment of Ivy Poisoning, New England M. Monthly **17**:270-272, 1898.

Test 2.—To one of two patches of dermatitis, saturated solution of magnesium sulphate (Squibb's) was applied on gauze, covered with rubber tissue, and a bandage. A similar dressing was applied to the control, using water in place of magnesium. After twenty-four hours, while the first patch was not healed, it was free from itching, was not tender, and not edematous, thus contrasting with the control, which remained tender for six days.

HOSPITAL CASES

A. B., male, aged 23, was poisoned four days previously. Whole face was edematous and the right eye closed. On Oct. 25, 1911, in the afternoon, hot applications of 2 per cent. permanganate were begun, but applied only to the right side of the face. In thirty hours the right eye was in good condition. The left side recovered tardily.

B. C., male, March, 1912, face and hands severely poisoned. The right side of the face and the right arm were treated with the hot permanganate, while the opposite side was treated with hot standard photographer's solution of sodium hyposulphite. In addition, both arms were bandaged in their respective solutions. After twenty-four hours the patient stated that the permanganate side felt distinctly better than the other. The right side recovered the earlier.

E. U., male, aged 25, was poisoned four days previously. Both arms showed marked edema, vesicles and pustules. He had already applied cold permanganate six or seven times. Hot permanganate was applied frequently by the nurse. There was no improvement in forty-eight hours. When the solution was changed to hot mercuric chlorid, and bandaging begun with the same, recovery began.

This case illustrates the uselessness of permanganate when the vesicles become infected.

A. E., male, aged 45. Dermatitis one day old. The whole face was swollen. The eyes half closed by edema of both lids. The right ear was much swollen. Thirty hours after the dermatitis began, hot permanganate saturated solution was applied to all areas. The application burned severely, especially the eyelids. Recovery occurred in five days, though this man had always been two weeks getting well. A weaker solution of permanganate would have been better.

Besides the results of Bigelow, Cantrell and von Adelung little can be attempted in summarizing the comparative values of these remedies as the results obtained by different physicians with the same remedy are so often conflicting.

One of the chief reasons for this unsatisfactory condition is the fact that many physicians in treating a case of rhus dermatitis will first use a so-called remedy for a few applications; failing to secure a satisfactory result this remedy will be replaced by another. This process may continue until finally convalescence, delayed or accelerated by the use of the various remedies, occurs and the remedy used in the last stages of the disease is considered the best. This remedy may then be used by another physician or the same physician in the initial stages of another case with failure as a result. A condition of disputation and uncertainty

results. In support of this explanation there are the published cases of Bartlett [87] (1838), French [88] (1903), Matheson [89] (1874), Morris [90] (1897), and Stone [91] (1874).

A further discussion of remedies will be taken up in a paper on the chemotherapy of rhus dermatitis.

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87. Bartlett, E.: Use of Chloride of Soda in Cases of Poisoning with Rhus Radicans, Boston M. & S. J. **18**:303, 1838.

88. French, J. M.: Rhus Toxicodendron and Rhus Poisoning, Merck's Arch. **5**:223-225, 359, 1903.

89. Matheson, A. C.: Treatment of Poisoning by Rhus Toxicodendron with Linseed Oil and Lime Water, Am. J. M. Sc., N. S. **67**:118, 1874.

90. Morris, E. K.: Guaiacol in Rhus Poisoning, Med. News **70**:57, 1897.

91. Stone, I. S.: Poisoning by Rhus Toxicodendron, Am. J. M. Sc., N. S. **67**:569, 1874.

CORRECTION

In the article by Dr. Robert S. Hodges on "Ringworm of the Nails," which appeared on page 1 of the July issue, on page 25, line 4 should read "attacking the nails."

Editorial

THE DERMATOLOGICAL RESEARCH INSTITUTE

News comes that the Dermatological Research Laboratories is hereafter to be called the Dermatological Research Institute. This change in name is probably an expression of the realization of ambitions to make this a permanent institution of research in dermatology, and the change in name has been accompanied by an act of honorable scientific altruism that is worthy of comment.

Dermatologists, and a few others perhaps, are familiar with the story of the Dermatological Research Laboratories. It was founded and supported for a few years by a rich benefactor for the purpose of making researches in psoriasis. In this work it developed a scientific staff which was capable of producing arsphenamin. When the war came on and the German supply failed us, this laboratory was able to supply the deficiency, and it was not only able to keep us from getting out of this drug, but to supply a better quality than we had had, and at a lower price. It did more than this: it was able to stabilize the situation after we got into the war, and to establish a price for this article, and a standard of quality, which probably we would have been unable to obtain had this institution not existed. Since the war it has been one of the producers of this drug, and has been foremost in the activities for its improvement.

Incidentally, in this course it has made money, and it is on its action in connection with this accumulation of money that we feel comment should be made here. This surplus amounted to the very large sum of $511,000.00—over half a million dollars. Legally it was the property of Dr. Jay F. Schamberg, Dr. George W. Raiziss and Dr. John A. Kolmer. At a meeting of the directors of the Dermatological Research Laboratories, March 3, 1921, Dr. Schamberg, Dr. Raiziss and Dr. Kolmer transferred this sum to the Dermatological Research Institute for, to use their expression, "the common good"; which evidently means for the support of this institution of dermatologic research. At no time in the history of the laboratory has there been any division of profits among these men in any form whatever. They received salaries, and the highest one, which did not go to the director, was less than the recipient could have earned elsewhere.

An act so handsome speaks for itself, and we shall not attempt to express our admiration for it. The Dermatological Research Institute deserves a long and useful existence.

W. A. P.

Abstracts from Current Literature

SILVER SALVARSAN IN TREATMENT OF SYPHILIS. C. M. WALSON, Am. J. Med. Sc. **161**:418 (March) 1921.

This is a report on work done with this preparation by the American Army Medical Corps in Germany. A review of the drug and its properties is given with the statement that its effect on the spirochete and its manifestations is slower with all silver salts than with neo-arsphenamin but the silver salts are less toxic and can be employed in larger doses. By animal experimentation the effectiveness of silver arsphenamin (silver salvarsan) is twice that of arsphenamin and three times that of neo-arsphenamin, the silver salt being arsphenamin plus silver, 0.25 gm. of the latter equaling 0.4 gm. of the old arsphenamin.

Emphasis is laid on having the solution well diluted, 0.1 gm. of the drug to 10 or 20 c.c. of doubly distilled water at room temperature, the injection taking at least two or three minutes. Great care should be used to prevent contact of the solution with the tissues.

Dosage will vary from 0.05 gm. to 0.1 gm. in initial doses up to 0.25 to 0.3 gm. toward the end of a course, injections being made every four days for six or eight doses. No more than 2 gm. should be given in one month.

The course of treatment recommended for the cure of syphilis consisted of four courses of silver arsphenamin and mercurial oil (the manufacturers state that mercury may not be necessary). One month is allowed to elapse between the first and second courses, each of seven doses, two and one-half months between the second and third, three months between the third and fourth.

In a series of 133 primary cases in which the lesion had existed from one to thirty days, 62 per cent. always gave a negative Wassermann reaction. Thirty-eight per cent. developed from a mild to a ++ reaction during the course of treatment. In a series of sixty-one cases of secondary syphilis all patients gave a negative Wassermann reaction after the first and second course of treatment.

The question of the use of mercury and silver arsphenamin together is not yet definitely decided, as some observers state that the two should not be used at the same time as the mercury may do harm and is superfluous, while others claim that they should be used conjointly as the mercury does no damage. All observers agree that the action of silver arsphenamin on lesions and spirochetes is prompt, and may be even more rapid than the action of arsphenamin, and that the effect of the drug is favorable in all grades of syphilis.

There is the possibility of anaphylactoid and angioneurotic symptoms in treatment with silver arsphenamin, but this could be avoided in general by the use of a small dose at the beginning of each course of treatment.

In a series of over 6,000 injections of silver arsphenamin, only two patients had arsenical poisoning which could be attributed to silver arsphenamin.

Albuminuria is not mentioned in cases in which silver arsphenamin alone was used, but it is possible that it may occur.

In general, some observers assert that silver arsphenamin is better than any other arsphenamin; some think it equal in value; while others think it produces no better results or even may prefer old arsphenamin to the new preparation.

It has not been proved that silver arsphenamin is better than arsphenamin, or that its use will replace arsphenamin and mercury in the treatment of syphilis.

JAMIESON, Detroit.

BENIGN GASTRIC ULCER IN A KNOWN SYPHILITIC. A RÉSUMÉ OF THE LITERATURE CONCERNING THE DIAGNOSIS OF ORGANIC GASTRIC SYPHILIS. W. FRANK FOWLER, Surg., Gyn. & Obst. **32**:419, 1921.

Fowler's summary and conclusions follow: Organic gastric syphilis is more frequent than formerly supposed. The gross lesions of gastric syphilis are (1) gummas in various forms, and (2) diffuse infiltration. Specific ulcers result from the degeneration of gummas. Symptomatically such lesions differ from benign ulcers, chiefly in the absence of pain, ease from food and alkalies, less periodicity, anacidity, vomiting, with good appetite, excessive weight loss and improvement in gastric function with specific treatment. Without operation the diagnosis usually rests on the past history of early syphilis, present late syphilitic signs, Wassermann reactions and the therapeutic test. However, a negative Wassermann reaction does not exclude the possibility of gastric syphilis, and benign lesions of the stomach may occur in a known syphilitic patient. At operation specific ulcers are always multiple, ragged lesions occurring usually at the cardia, the lesser curvature, or the pyloric region accompanied often by perigastric adhesions, thickened gastric walls and gastric deformity. Large gummatous tumor masses or cicatricial contractions subsequent to extensive ulceration simulate carcinoma, particularly as regards the type of dyspepsia, the vomiting, the rapid loss in weight, and the anacidity, although the cachexia and loss of strength are less than that encountered in malignancy, and the course may have been longer. The operative findings consist usually of an irremovable gastric tumor mass indistinguishable from carcinoma. The roentgen-ray evidence also simulates carcinoma. The roentgenographic signs of gastric syphilis in general consist of encroachments on the lumen, distortions and deformities. The microscopic evidence consists of the characteristic syphilitic obliterative endarteritis and perithelial lymphocytic infiltration with atrophy of the mucous membrane and hypertrophy of the submucosa and muscularis. Postmortem confirmation of the diagnosis is infrequent.

Organic gastric syphilis may simulate (*a*) benign gastric ulcer, (*b*) gastric carcinoma, or (*c*) present an atypical gastric picture.

The diagnosis of organic gastric syphilis is often difficult and sometimes impossible.

A negative Wassermann reaction does not disprove the existence of syphilis, and a positive reaction does not prove that a gastric lesion is specific.

The therapeutic test is usually reliable but not infallible.

The roentgenographic evidence is not conclusive.

Exploration may not be determinative, particularly as regards differentiation from carcinoma.

Atypical, chronic gastric disorders, which are unresponsive to the usual treatment, should arouse suspicions of syphilis.

Fowler adds a case to his report of a gastric ulcer in a woman of 26, who did not respond to antisyphilitic treatment, although she was an undoubted syphilitic. Previous operations on this patient had given but temporary relief, and the pyloric half of the stomach, together with some large lymph nodes in the gastro-colic omentum, were removed. The pathologic examination showed a gastric ulcer with fibrous base, chronic inflammatory changes, and lymphadenitis in mild degree.

GOODMAN, New York.

THE CONSTITUENTS OF CHAULMOOGRA OIL EFFECTIVE IN LEPROSY. J. T. McDONALD and A. L. DEAN, J. A. M. A. **76**:1470 (May 28) 1921.

For fourteen and one-half months, a period ending the middle of March, 1921, the authors have been able to observe a series of patients with leprosy treated by their "standard treatment." This standard treatment consists of weekly intramuscular injections of the mixed ethyl esters of chaulmoogra oil carrying 2 per cent. of iodin in chemical combination. This is supplemented by the oral administration of the fatty acids and combined with 2.3 per cent. of iodin.

The following table shows the results of this treatment.

RESULTS OF TREATMENT

Number of patients, Jan. 1, 1920	72	
New patients received, Jan. 1, 1920 to March 15, 1921	116	
Total number of cases		188
Deaths	7	
Paroled	94	
Total departures		101
Patients on hand, March 15, 1921		87

The authors' clinical observations appear to establish the fact that oral administration of chaulmoogra oil compounds are of doubtful value. Patients receiving injections alone did as well as those receiving combined treatment. They also believe that the therapeutic activity of chaulmoogra oil resides in the contained hydnocarpic and chaulmoogric acids. Patients treated with these acids in a pure state improved with the same rapidity as did those receiving the standard treatment. The authors state that "the fatty acids of the chaulmoogric series are specific in leprosy." Iodin appears to possess little therapeutic efficiency in leprosy.

Investigations at Kalihi Hospital have brought to light another substance in chaulmoogra oil which appears to possess the carbon ring characteristic of the chaulmoogric series, but is more highly unsaturated than either chaulmoogric or hydnocarpic acids. Clinical tests with this material indicate that it is particularly efficient therapeutically. However, investigation of it has not proceeded far enough to determine its true value.

MICHAEL, Houston, Texas.

USE OF PEPSIN IN DERMATOLOGY. F. P. CEPELKA, Ceska dermat. **2**:92, 1921.

The use of a digestive mixture of pepsin and hydrochloric acid originated with Unna. His therapy is based on the fact that only the superficial layer of horny cells resists digestion, while the body of the cells consists of poorly digestible keratin B and easily digestible albumoses. In the cutis, the plasma and the connective tissues undergo digestion rapidly. Unna used his digestive mixture most successfully in the treatment of keloids, as they consist mostly of pathologically changed connective tissue. He also obtained good results in the treatment of hypertrophic scars from burns, lupus ulcers, acne indurata, lymphatic indurations and adenitis. The mixture controlled well exuberant granulations and cleaned and deodorized necrotic tissues. It makes a painless keratolytic for keratoma.

Unna's original formula is:

		Gm. or C.c.
℞	Pepsin	10
	Hydrochloric acid	
	Phenol āā	1
	Distilled water ad	200

Later, for safety's sake, Unna reduced the amount of pepsin to 1 per cent. The digestive mixture is applied in the form of wet compresses, strictly limited to the treated area, and covered with impervious material. It is advisable to protect the surrounding skin by some bland ointment.

In view of the fact that during the process of digestion the cells become porous, and thus an osmosis takes place, it is possible to make use of this method to introduce into the skin, by means of osmosis, the substances to which the horny layer is otherwise impermeable, such as epinephrin, morphin, cocain, arsenic and other drugs.

Wassermann modifies Unna's technic. He advises the admixture of 10 per cent. pyrogallcollodium. Pepsin aids pyrogallol to penetrate, while collodium assures a localized application.

At the clinic in Prague the original Unna's technic is used with good and indifferent results. It was found most effective in the treatment of keloids and hypertrophic scars. Keloids flatten out, scars become more pliable, contractures stretch and give considerably. It is a long and drawn-out procedure in many cases, requiring a good deal of patience, but as it is often the only possible treatment at hand, it is worth trying. Care must be taken to stop short of irritation. The success depends to a large extent on careful application.

CEPELKA, Chicago.

DIAGNOSIS OF SYPHILIS AND GLAND PUNCTURE. H. DROOP, Dermat. Ztschr. **32**:336, 1921.

The method of gland puncture for the diagnosis of early syphilis was first proposed by Hoffmann. The method is especially valuable in cases of inaccessible primary lesions, as when accompanied by phimosis, if the lesion has been treated, and if the demonstration of the spirochetes is complicated by types of organisms which simulate the *Spirochaeta pallida* and add confusion to bacterial diagnosis. Such organisms include the *S. refringens*, and certain so-called "intermediate forms" as *S. gracilis, pseudo-pallida, dentium*, etc.

Although spirochetes have been demonstrated in the glands in other conditions than syphilis, Castellani, for example, having found organisms similar to *S. pallida* in 50 per cent. of patients with frambesia, ordinary diseases in which the spirals have been said to exist, lung gangrene, lymphatic leukemia, Hodgkin's disease and lymphosarcoma add but little concern in differential diagnosis.

Droop examined the lesions of fifty patients with primary syphilis and of five with secondary cases. Of the primary cases *Spirochaeta pallida* was demonstrable in twenty-seven; an examination was not made in four; twice the examination was accepted as negative after one dark-field investigation; ten times the primary lesion could not be studied on account of accompanying phimosis. Seven times the examination was negative due to some local application.

Gland puncture in these fifty cases gave thirty-eight positive and twelve negative results. In the ten cases of phimosis, the spirochetes were demonstrated nine times; in five positive gland examinations, the concomitant lesion examination was negative. Droop notes that the positive diagnosis in fourteen cases of fifty depended on gland puncture.

GOODMAN, New York.

FURTHER CONTRIBUTION TO KNOWLEDGE OF RELATION OF ENDOCRINE GLANDS. JAROSLAV JEDLICKA, Ceska dermat. **2**: Nos. 5-6.

(*a*) *A Case of Geroderma.*—The cases described in the literature under the names of geroderma, senilismus, senium praecox and progeria are not identical in details, each having its own peculiarities. They appear at different ages and from various causes, but clinically they all manifest themselves by premature old age with its senile degenerative cutaneous changes, premature grayness and loss of hair, and impaired sexual power. The disease is the outcome of a pluriglandular insufficiency with main changes in the thyroid and sexual glands. The author cites a case of a man of 36, aging beyond recognition within twenty months (apparently), without any other cause but war hardships. Besides senile appearance he showed lowered sexual power, general asthenia, paresthesias, tremor of extremities, a lowered nitrogen metabolism and increased carbohydrate tolerance. The patient improved remarkably under thyroid therapy.

(*b*) *Case of Myxedema Idiopathicum Adultorum.*—A woman suffering for twenty-one years from hypothyroidism showed all the typical consequences: The trophic changes in all ectodermal structures, a lowering of all vital processes and of general metaoblism and physical changes. As a complication she had polyneuritis and anemia with lymphocytosis. The case illustrates besides the hypothyroidism a coexisting hyperpancreatism with high carbohydrate tolerance, and a lowered epinephrin glycosuric effect. It proves again that the thyroid stimulates the chromaffin system and antagonizes the action of the pancreas.

(*c*) *Exophthalmic Goiter and Diabetes.*—A middle-aged woman who had suffered with exophthalmic goiter for three years developed a severe case of diabetes and died. The case is cited as a contrast to the first two cases: Hyperthyroidism led to hypopancreatism and an increased function of the suprarenals. Hypersuprarenalism increases the sugar concentration in the blood, and the coexisting hypopancreatism still further interferes with the combustion of the sugar. The cause of glycosuria is, therefore, complicated.

CEPELKA, Chicago.

REGARDING DIFFUSE CONGENITAL HYPERKERATOSIS. J. Golay, Ann. de dermat. et syph. **3**:97, 1921.

A girl, 3 weeks old, had been born with a brownish-yellow skin which markedly resembled a coat of collodion. It was fissured in places. The flexor surfaces were the more markedly involved; beyond ectropion of the lids there was no deformity. The sparse hairs of the scalp were unusually long. Minute sebaceous cysts appeared on the nose. Treatment with a bland ointment was instituted, but no relief was obtained, and the child died a month later with bronchial pneumonia. Necropsy revealed little of interest. A complete report is given, including the histologic examination of the skin.

The author considers congenital hyperkeratosis distinct from ichthyosis vulgaris, although at present they cannot be definitely distinguished histologically. The sites of predilection are exactly opposite. The congenital hyperkeratosis is present at birth, while ichthyosis vulgaris develops later, and is not congenital but hereditary. The former is usually incompatible with life; the latter is never. This congenital condition or malformation belongs probably in the same group as erythroderma ichthyosiforme and keratosis palmaris et plantaris.

The condition described may be due to tuberculosis in the mother, or to syphilis, or to a consanguineous marriage, but it is more probably toxic in origin. In the present case the child's mother had, during her pregnancy, consumed large quantities of salt to satisfy a craving. This she had also done during three of her six previous pregnancies, and all three had resulted in fetal hyperkeratoses and death at birth or soon after. The other children showed no trace of the condition. The author thinks that the salt may have had an ill effect on the kidneys, causing the circulation of toxic substances which influenced the fetal development. This is offered merely as a theory, to be tried in future work.

Parkhurst, New York.

TREATMENT OF PARESIS AND TABES. Wagner-Jauregg, Wien. klin. Wchnschr. **34**:171, 1921.

As early as 1887, the author has noted that remission of paresis seemed to have been preceded by some acute febrile disease. He suggested that this phenomenon might be used therapeutically. A few years later (1890) he used Koch's tuberculin in conjunction with mercury and obtained very favorable results. More recently, he has used Besredka's typhoid vaccine to cause a febrile reaction, with equally good results. In 1917, he tried the injection of the parasites of tertian malaria. During the last two years he has used this method in a large series. He injects whole blood from a patient with malaria into the subcutaneous tissues of a paretic patient. After an incubation of from five to thirty-one days, typical chills and fever paroxysms occur. The temperature rises as high as 40 to 41 C. After eight or more paroxysms, the malaria is treated with intravenous injections of quinin, and simultaneously six injections of neo-arsphenamin at weekly intervals are given. With this treatment every patient with induced malaria has been cured. The results on the paretic symptoms have been better with this mode of therapy than with any other known to Wagner-Jauregg. He says it is interesting that the serologic and spinal fluid tests do not parallel the clinical course of the improvement.

The limitations to the method are that it can only be executed where there is endemic malaria, or else where the number of paretic patients is so great

that the plasmodian can be propagated among the paretics themselves. In this way the author has obtained about twenty-six successful passages of the malarial parasite.

GOODMAN, New York.

CASE OF EPIDERMOLYSIS BULLOSA. DR. SCHWANK, **2**:30, 1920.

A man, aged 28, with a tuberculous and neuropathic family history, who was tuberculous and neuropathic himself, showed symptoms of vasomotor disturbances, dermographism, acro-asphyxia, hyperhidrosis, and other conditions. According to the patient's story, his mother, one aunt, one sister and two brothers suffered from the same skin trouble he had, the main symptoms of which was weeping, recurring in the fall, lasting two to three months and disappearing spontaneously. The patient has had recurrences since he was 3 years old. The present attack was the most severe, localized, however, only on the left lower extremity. Vesicles first appeared in places bitten by a mosquito. New crops followed on the skin irritated by scratching and pressure of clothing. Vesicles came on without prodromal symptoms usually at night. Lesions healed without trace. It was possible to produce new vesicles experimentally by prolonged rubbing or pressure. Sudden trauma, no matter how intense, failed to produce them.

The author reviews the pathogenesis and etiology of epidermolysis bullosa. The patient in this case was tuberculous. His suprarenals also might have shown tuberculous changes with consequently altered secretion, possible irritation of capillaries, and increased lymph secretion. Weeping goes on indefinitely under an intensive irritation of vasodilations. The rapid response to treatment in this case would uphold the correctness of the theory. After the third injection of epinephrin (0.5 c.c. of 1:1,000) the weeping stopped completely. After five injections the lesions dried up and healed. Even the general condition improved, the patient losing his sensation of fatigue and depression. Once during the observation there was a marked improvement following a sexual excess. Cases of this type are probably the result of a combined disturbance of the glands of internal secretion.

CEPELKA, Chicago.

ANTISYPHILITIC THERAPY. A COMPARATIVE STUDY OF SOME INTENSIVE METHODS. LOUIS CHARGIN, J. A. M. A. **76**:1154 (April 23) 1921.

Chargin studied the effect of three plans of intensive antisyphilitic therapy on 106 cases of early syphilis. These patients all presented early cutaneous manifestations of the disease and a strongly positive (+++ to ++++) Wassermann reaction.

Thirty-seven were treated according to the method advocated by Pollitzer; that is, three full doses of arsphenamin were given on three successive days followed by six weekly injections of an insoluble mercurial salt. Nineteen patients received three or four injections of arsphenamin on alternate days, followed by six weekly injections of mercury, and this in turn by additional administrations of arsphenamin, three, four or five in number, a week apart or on alternate days. Fifty patients were given from six to eight injections of arsphenamin five days to a week apart, combined with ten to twelve injections of mercury at weekly intervals.

Wasserman tests were made at weekly intervals on all patients, and the results of the tests were used as a criterion of the efficacy of the method. So far as the clinical manifestations of the disease were concerned, each of these programs caused their disappearance with equal rapidity.

As a result of the study, it was found that the most intensive method had no advantage over the less intensive ones, and Chargin, therefore, concludes that the latter are to be preferred since they offer a greater margin of safety.

MICHAEL, Houston, Texas.

CONTRIBUTION TO THE DIFFERENTIATION OF GRANULOMATOUS SKIN DISEASES. L. ARZT, Acta dermat.-ven. **3-4**:365 (Dec.) 1920.

In April, 1913, a man, aged 25 years, appeared with an ulcer, 3 by 10 cm. in size, located in the right occipitonuchal region. It had started a year previously, heralded by an enlargement of the cervical lymph nodes, and had spread progressively in spite of local treatment, including the roentgen ray in semi-intensive doses. The ulcer had sharp, firm borders and a rough, purulent, necrotic base, reaching the bone. There were palpable lymph nodes in the neighborhood. The blood findings were normal, except an eosinophil count of 5 per cent.; the tuberculin reaction was negative; no tubercle bacilli or other apparently causative organisms could be found; syphilis was excluded by the therapeutic test; the favored guess was "mycosis fungoides d'emblée." With febrile exacerbations the ulcer extended, involving muscle and bone; there was considerable sloughing. The bacillus of glanders was sought in vain. There soon followed a lethal exitus. Necropsy revealed the presence of a granulomatous process with circumscribed nodules in the lymph nodes, liver and spleen. Here, as well as in a section from the ulcer, were found lymphocytes, plasma cells and large polygonal cells like those described by Paltauf and Sternberg. It was, therefore, a case of lymphogranulomatosis with ulcus lymphogranulomatosum. The primary involvement was probably in the lymph nodes rather than in the skin. This process stands near mycosis fungoides, especially the form d'emblée, in classification, but the necropsy and histologic examination easily show its distinguishing characteristics.

The discussion is interesting and the bibliography good.

PARKHURST, New York.

ETIOLOGY OF SARCOIDS OF BOECK-DARIER. B. REJSEK, Ceska dermat. **1**:113, 1920.

The majority of dermatologists believe that sarcoids or so-called tuberculids appear in persons suffering from manifest or latent tuberculosis. Tuberculids are caused either by the action of toxins (toxic theory), or by bacilli brought to the skin by the blood current or introduced into the skin from without (bacillary theory). Bacilli lodging in the skin are either usually dead or incapable of multiplication. Rarely they reach the skin alive, and in that case cause genuine tuberculosis of the skin with positive findings of the organisms in the sections.

The author believes that the blood of a patient suffering from latent or manifest tuberculosis always contains a certain number of toxins which may vary from time to time. If the variation takes place gradually the skin has time to adjust itself, while at the same time it becomes hypersensitive to all

other conditions. If the concentration of toxins increase suddenly, a reaction takes place with the formation of some form of tuberculid without the direct action of the tubercle bacillus. Different types of tuberculids can appear at the same time. The number of lesions depends on the number of toxins produced above the tolerated concentration. The author's case illustrates the simultaneous appearance of lichen scrofulosorum on the face and miliary lupoids of Boeck-Darier on the body in a woman with active pulmonary tuberculosis. The article contains a detailed description of lesions with histologic findings.

CEPELKA, Chicago.

ICTERUS SUPERVENING TWO MONTHS AFTER ARSENICO-MERCURIAL TREATMENT IN A CASE OF SECONDARY SYPHILIS. RESUMPTION OF ARSENICO-MERCURIAL TREATMENT. GRAVE ICTERUS. LETHAL EXITUS. P. RAVAUT, Bull. soc. franç. de dermat. et syph. **2**:57, 1921.

A girl, aged 18, had a genital chancre and a secondary eruption. She was first given mercuric cyanid (1 c.c. of a 1:100 solution, intravenously) daily for five days. Then weekly injections of neo-arsphenamin were begun and she received eight of them in doses increasing from 0.2 gm. to 0.75 gm. with fourteen injections of the cyanid interspersed. A slight urticaria followed the first injection of neo-arsphenamin. At the end of this course an acute anginal infection occurred; during convalescence eight injections of strychnin cacodylate were administered; icterus appeared with chills, nausea and vomiting. The administration of calomel brought no relief, small doses being employed. The liver was large and tender, and there was some splenic enlargement. Antisyphilitic treatment was resumed, with seven injections of mercuric cyanid (as above) and two of neo-arsphenamin (0.1 and 0.2 gm.). There was an exacerbation, two more small doses of neo-arsphenamin were given, and the patient soon died in coma. No spirochetes could be found in the liver, and it was concluded that there had been a toxic hepatitis, possibly due to arsenic.

PARKHURST, New York.

EFFECT OF INTRAVENOUS ADMINISTRATION OF ARSPHENAMIN, NEO-ARSPHENAMIN AND MERCURY. ROBERT A. KILDUFFE, J. A. M. A. **76**:1489 (May 28) 1921.

This investigation was actuated by the recent report of Strickler, Munson and Sidlick on the effect of arsphenamin on the Wassermann test in non-syphilitic patients. It will be remembered that these workers reported the production of positive complement fixation following the intravenous injection of arsphenamin.

Kilduffe used rabbits whose serum was consistently Wassermann negative. To one set of animals he gave three intravenous injections of arsphenamin solutions in doses of 0.01 gm. per kilogram of weight, equivalent to 0.6 gm. per 60 kg., or the weight of a young adult. The second series received three intravenous injections of neo-arsphenamin solution in doses of 0.02 gm. per kilogram of weight, equivalent to 1.2 gm. per 60 kg. A third series received intravenous injections of solutions of mercuric chlorid in doses of 0.00033 gm. per kilogram of weight, equivalent to 0.0193 gm. per 60 kg.

The drugs were given at weekly intervals and blood for Wassermann tests was taken just prior to each injection.

The results were uniformly negative, a positive Wassermann reaction not being produced in any animal of any series. Kilduffe believes that these findings are significant and indicate the necessity for further investigations of this subject.

MICHAEL, Houston, Texas.

WHAT ARE PARTS PLAYED BY MERCURY AND BACTERIA RESPECTIVELY IN PATHOGENESIS OF MERCURIAL ULCERATIVE STOMATITIS AND COLITIS? J. ALMKVIST, Acta dermat.-ven. **3-4**:312 (Dec.) 1920.

In an exhaustive article with an extensive bibliography, the author thoroughly considers this question, and arrives at these conclusions:

1. The bacteria acting in mercurial ulcerative stomatitis and colitis are not specific bacteria, but albumin-decomposers of various kinds.

2. These bacteria play their rôle in a two-fold manner: First, by the process of decomposition, they give rise to local erosions of the mucous membrane and a local formation of hydrogen sulphid which, together with the mercury in the tissue, produces local tissue necroses. Second, they convert the tissue necroses that have arisen into putrid progressive ulcerations.

3. The rôle of the mercury is this: In combination with the locally absorbed hydrogen sulphid gas, it causes intercellular mercury sulphid deposits in the endothelial cells of the capillaries which, by damaging these cells, check the formation of the tissue fluid, thereby provoking local tissue necroses. These tissue necroses improve the substratum for the bacteria which multiply in it enormously, their virulence being thus increased so that they are able to attack healthy tissue. The final outcome of mercurial action is, in other words, a powerful furtherance of the development of the albumin-decomposing bacteria.

PARKHURST, New York.

CONSIDERATIONS REGARDING CLINICAL VALUE OF BORDET-WASSERMANN REACTION. C. ABADIE, Bull. Soc. franç. de dermat. et syph. **2**:54, 1921.

The results of the Wassermann test do not coincide with our present conception of the laws of immunity; we have only a vague idea of its significance. It is therefore urged that we interpret its results only in the light of all the clinical findings assembled. Undue reliance must not be placed on it, in diagnosis and especially in treatment.

PARKHURST, New York.

NEW CONCEPTIONS RELATIVE TO THE TREATMENT OF MALIGNANT DISEASE, WITH SPECIAL REFERENCE TO RADIUM IN NEEDLES. W. L. CLARK, Pennsylvania M. J. **24**:214 (Jan.) 1921.

Clark states that the use of radium needles has revolutionized radium technic. Results are obtained by this method that cannot be secured by the application of radium in plaque or capsule. The needles are particularly efficacious in the treatment of growths too large for radium penetration from the outside by capsule or plaque. With the newer method malignant growths situated in the intestines, omentum, larynx, frontal sinus and other locations difficult of access, are not entirely hopeless.

Clark uses needles made of "noncorrosive steel," of various length and style of point, all having a wall thickness of 0.3 mm. Each contains from 5 to 10 mg. of a radium salt.

No definite rules of technic can be given since every case is a law unto itself. Generally speaking, needles are placed in sarcomatous tissue 20 mm. apart and withdrawn in twelve hours. In carcinomas, the needles are placed 25 mm. apart and removed in from eighteen to twenty-four hours.

The use of radium needles is only in its infancy; yet even without definite knowledge as to technic, a great deal has been accomplished. The future will show this method to be of even greater potency.

MICHAEL, Houston, Texas.

HYPERKERATOSIS EXCENTRICA. J. BUKOVSKY, Ceska dermat. **2**:61, 1920.

The author reports a case of hyperkeratosis excentrica that showed all the typical symptoms of the condition as described by Mibelli under the term of porokeratosis. The article contains a histologic study of the skin findings, especially the early changes. The author arrives at the following conclusions: From an unknown cause, areas of porokeratosis appear early in life in different localities. These centers of porokeratosis become more numerous with each attack. Each center first appears as a tubercle enlarging peripherally. After a varying length of time, the oldest part of the condition begins to desquamate and the lesions assume a new form—a deepened scaling center with a porokeratotic, hard border without desquamation. If the scaling reaches the periphery, the entire lesion flattens out and becomes barely noticeable; a recurrence may, however, take place. The course of the disease may last for years; even changes in individual lesions take place slowly. The treatment is ineffective, ameliorations being only temporary.

The author believes that the term "porokeratosis" is ill-fitting, and prefers Respighi's name "hyperkeratosis excentrica" or Respighi and Dyerea's term "hyperkeratosis figurata centrifuga atrophicans."

CEPELKA, Chicago.

SOME EXPERIMENTS ON THE VOLATILIZATION AND ABSORPTION OF MERCURY. C. E. JENKINS, Brit. J. Dermat. & Syph. **33**: 135 (April) 1921.

Jenkins conducted experiments on the volatilization of mercury at blood heat, placing the metal in incubators kept at that temperature, and found no volatilization of the metal.

A second set of clinical experiments was conducted, four patients being given mercury inunctions under conditions which allowed little opportunity for inhalation of any of the metal which might have been volatilized, and the author feels that the onset of mercurialism was as rapid as one could expect after inunction in the usual way.

He therefore concludes that the rate of volatilization of mercury at blood heat is insignificant, and that in the inunction method of administering mercury the metal is absorbed through the skin.

SENEAR, Chicago.

CASE OF SYPHILITIC REINFECTION. H. BREIDE, Acta dermat.-ven. **3-4**:456 (Dec.) 1920.

A man, aged 25 years, was seen July 25, 1917, with a chancre in which the spirochetes of syphilis were found. He received ordinary mixed treatment, with neo-arsphenamin and mercurial injections for four courses.

June 24, 1920, he and a comrade were exposed with the same woman, and three or four weeks later a genital ulcer appeared, not in the location of the lesion of 1917. There were the typical satellite lymph nodes in the groin, and *Spirochaeta pallida* was found in the ulcer. The Wassermann reaction was negative, and continued so during treatment, which was energetic.

(In this same issue, under the heading, "Clinical Reports," Almqvist publishes two cases of syphilitic reinfection. Both occurred in men who transmitted their first infection to their consorts, were apparently cured, and then presented new initial lesions, having had no extra-marital intercourse in the interim.)

PARKHURST, New York.

IODIN IN CEREBROSPINAL FLUID, WITH SPECIAL REFERENCE TO IODID THERAPY. E. D. OSBORNE, J. A. M. A. **76**:1384 (May 21) 1921.

Kendall's method was employed in this investigation. Iodin was found in normal cerebrospinal fluid in an average amount of 0.018 mg. per 100 c.c. None of the patients on whom this determination was made had received any therapy by mouth for the previous three or four months.

Increased amounts of iodin were present in the cerebrospinal fluid after the administration of potassium iodid by mouth and rectum and following the injection of sodium iodid intravenously. After the latter method of introducing the drug, a definite curve of the iodin content of the cerebrospinal fluid can be plotted. This curve depends on the amount administered.

In four neurosyphilitic patients who were receiving sodium iodid intravenously, large amounts of iodin were found in the cerebrospinal fluid. The fluid from one patient contained 42.308 mg. per 100 c.c., while the others approximated 4.5 mg. for the same amount of fluid.

These four observations point to one or both of two possibilities: either the meninges are more permeable to iodin compounds when there is meningitis or tissue actively involved by syphilis takes up more iodin than normal tissue.

MICHAEL, Houston Texas.

RECURRENT PHLYCTENULAR ERUPTION ON EXTREMITIES WITH MENINGEAL REACTION. L. CHATELLIER, Ann. de dermat. et syph. **3**:151, 1921.

In 1914, a man of 21 years, first noticed on his hands an outbreak of vesicles which lasted several weeks, accompanied by a tingling sensation. The attacks continued at intervals of a few weeks. According to the history, the grandmother and an aunt had previously suffered from similar trouble.

The lesions were found to be vesiculopustular, involving the nails as well as both surfaces of the hands. There was no itching. Redness and desquamation were features. The blood showed a small mononuclear leukocytosis, and the spinal fluid, though otherwise apparently normal, showed 24 lymphocytes per cubic centimeter. The lesions correspond to those of Hallopeau's "acrodermatite discontinue." There is given a brief review of similar cases in the French literature. The possibility of a relationship to erythema multiforme is considered, although the lesions here were essentially monomorphous and the subjective symptoms were slight; neither was there an eosinophilia. The meningeal reaction is remarkable.

PARKHURST, New York.

EOSINOPHILIA AND ITS RELATION TO SKIN DISEASES. V. SVESTKA, Ceska dermat. **1**:73 and 96, 1920.

The first part of the paper discusses the phenomenon of eosinophilia in general, its relation to infections and anaphylaxis. It reviews the theories about the origin of eosinophils from the bone marrow and possible transformation of neutrophils into eosinophils. The author believes in the possibility of extramedullary origin of eosinophils and in local histogenesis of eosinophilic cells in the skin and mucous membranes.

Svestka studied ten cases of scabies in regard to blood changes, and tabulated his results. Untreated patients show a high degree of eosinophilia (31.05 per cent. in Case 1). The number of eosinophilia cells decreased rapidly under treatment. Eosinophilia results from the irritation of the organism by toxic products of the vital activity of parasites, and will increase in proportion to their activity; it is independent of skin findings.

A high degree of eosinophilia was found in dermatitis herpetiformis (58 per cent.). At a certain stage of development the bullous lesions show eosinophil cells only; later neutrophilic leukocytes and lymphocytes also make their appearance. There is a direct relation between the temperature and blood eosinophilia, which is the highest at the height of fever.

CEPELKA, Chicago.

CURE OF MELANOTIC TUMOR AND MELANOTIC SPOTS BY MEANS OF RADIUM THERAPY. S. MENDES DA COSTA and J. PAPEGAAY, Acta dermat.-ven. **3-4**:309 (Dec.) 1920.

A woman, aged 84 years, had a tumor near the inner canthus of the eyelid and a spot, diagnosed lentigo senilis, on the nose. For fear of metastasis a biopsy was not made. A round, flat metallic plaque, 1.5 cm. square, containing 2.5 mg. of radium sulphate, was applied with a tin filter, 0.2 mm. thick, for six hours at a time, every two days for two weeks, then weekly for three treatments with 0.1 mm. of tin. Three months later two small black spots remained, which were treated twice for three hours through 0.05 mm. of tin and once for six hours through 0.1 mm., at intervals of one week. Not a trace remained, and there has been no recurrence in two years.

A girl of 20 years presented two black spots about the nose, of six and three years' duration, one appearing papular. Radium bromid, amounting to 10 mg., was applied with good results.

PARKHURST, New York.

INFLUENCE OF METEOROLOGIC CHANGES ON SKIN DISEASES. KAREL HUBSCHMANN, Ceska dermat. **2**:19, 1920.

Dr. Bettmann published in the *Münchener medizinische Wochenschrift*, 1920, No. 23, an article dealing with the unquestionable influence of meteorologic changes in the spring on the human organism, especially the increase in the growth of hair and nails, and increase in the secretory activity of sweat and sebaceous glands, depending probably on the increased activity of the glands of internal secretion.

Two cases of dermatitis exfoliativa generalisata observed at the hospital of Prague are described in a preliminary report of the author. They further illustrate Dr. Bettmann's observations, and show the changes in a dermatosis under varying atmospheric conditions. The first patient, a woman of 50, showed a definite undeniable aggravation in the skin condition, with a mental

depression from six to twelve hours before a sudden fall of atmospheric pressure. As she showed signs of hypothyroidism, she was put on thyroid therapy with wonderful success. Her condition cleared up completely. It is difficult to state whether, or to what extent, spring influenced this syndrome.

CEPELKA, Chicago.

CASE OF GLANDERS IN MAN. CLEMENT, Bull. Soc. franç. de dermat. et syph. **2**:63, 1921.

A member of the Corsican hussars contracted the disease from horses in his regiment. Signs of a general infection first appeared: fever, epigastric pain, vomiting, headache and general malaise. That which dominated the scene was a syndrome of suprarenal insufficiency, with marked hypotension. Some time later abscesses appeared successively on the left calf, the dorsum of the hand and the forehead. The first was evacuated, and the others were cauterized by heat. The bacilli were found in cultures. A few days later the face became greatly swollen, and there were fetid ulcerations of the cheek and hand. The patient became rapidly comatose and died, more than three months after the onset of the infection. A vaccine was prepared too late to be of service.

PARKHURST, New York.

A CASE OF ORIENTAL SORE (OF ITALIAN ORIGIN) ENCOUNTERED IN THE UNITED STATES. R. D. SPENCER, J. A. M. A. **76**: 1494 (May 28) 1921.

An Italian, aged 18, a recent immigrant into this country, had a large sore on his right cheek and two smaller but similar lesions on his left wrist. The lesions had all appeared while the patient was still living in Italy.

The sore on the face was 3 cm. in diameter; its margin was brownish red, slightly wavy and elevated, merging and fading into the surrounding normal skin, indurated and not painful on pressure. The base of the lesion was covered by a brownish crust, which when removed revealed a raw, red, granular bleeding surface.

Smears from the lesion showed numerous typical leishmanias. Cultivation was unsuccessful. Inoculations into a rabbit, a guinea-pig and a snake were without result.

Treatment with carbon dioxid snow was followed by prompt cure.

MICHAEL, Houston, Texas.

MULTIPLE CHANCROIDS IN CASE OF SCABIES. JAROSLAV POHL, Ceska dermat. **2**:77, 1920.

The patient was treated in the hospital for scabies. The second or third day after taking a bath in a tub previously used by the patients from the venereal ward, he noticed a small ulcer on the penis, soon two more in the same locality, and several others on the thigh. They developed into chancroids. The secretions and sections from the ulcers contained Ducrey-Unna's streptobacilli. The case illustrates the possibility of extragenital localization of chancroids in the course of other generalized dermatoses, especially scabies, with its many lesions of the epidermis. It is a well-known fact that a scabetic skin is susceptible to pyogenic infections and extensive impetiginous processes.

The macroscopic appearance in the given case might lead to difficulty in diagnosis. The chancroids do not respond to treatment as rapidly as a more superficial impetigo.

The patient's story (infected in the bath-tub) might have been truthful. Streptobacillus, just like the gonococcus and *Spirochaeta pallida,* can keep its vitality for a certain length of time in a moist medium. The case teaches the importance of the observation of strict hygienic precautions in venereal wards.

CEPELKA, Chicago.

SACHS-GEORGI REACTION AS A SUBSTITUTE FOR WASSERMANN REACTION. J. A. MURTO, Acta dermat.-ven. **3-4**:446 (Dec.) 1920.

In a series of 1,000 serums the author found that the two reactions agreed in 92.6 per cent. of cases. The new method seems especially valuable in diagnosing latent cases. The preparation and dilution of the extract is considered, this being the nucleus of the reaction. It is of course advantageous that the serum be fresh, although the author has obtained good results with serums four or five days old, and even six.

The reaction of Sachs-Georgi is much simpler of execution than the Wassermann test, and it seems as accurate and useful; it is also less expensive as regards materials. It is hoped that it may soon be substituted for the other, more arduous method.

PARKHURST, New York.

ON CREEPING DISEASE. HARUKICHI TAMURA, Brit. J. Dermat. **33**:138 (April) 1921.

The second part of Tamura's article considers first the clinical character of the line produced by the larva, and he describes erythematous, papular and vesicular types. He then discusses the histologic changes which have been found in the nine cases, including his own, studied from this standpoint. He again states that, while the *Gastrophilus* larva has been accepted as the cause of the disease, the *Gnathostoma* and *Hypoderma bovis* have now been found to be causative in some cases, and he predicts that other parasites will be incriminated in the future.

SENEAR, Chicago.

TWO CASES OF TABES WITH GASTRIC CRISES, TREATED BY NEO-ARSPHENAMIN. LEREDDE, Bull. Soc. franç. de dermat. et syph. **2**:47, 1921.

The first man, 35 years of age, was given 22.6 gm. of neo-arsphenamin during thirteen months, and the second, aged 48, received a total of 45.15 gm. in thirty-three months. In both cases the gastric crises were persistent at first and seemed to be aggravated by the treatment, but as the injections were continued the attacks became less and less frequent and finally disappeared entirely. Leredde emphasizes that treatment must be continued in spite of a pseudo-aggravation of symptoms. Even the mildest case, he says, must receive the most vigorous treatment, for the apparently mild cases are often harder to influence than the more severe. The treatment by daily injections (Sicard) is discouraged as productive of too much pain in these cases.

PARKHURST, New York.

PITYRIASIS RUBRA PILARIS. V. Svestka, Ceska dermat. **1**:126, 1920.

The author considers pityriasis rubra pilaris as a definite dermatologic entity and not a disease of the lichen group. His case, in a woman of 40, with otherwise negative findings, shows a well established clinical picture.

The author considers a disturbance of internaal secretions as the possible etiologic factor. The article is illustrated by three photomicrographs of sections from involved skin.

Cepelka, Chicago.

DERMATOLOGIC ABSTRACTS

The Journal of the American Medical Association

SYPHILITIC MASTITIS. R. Burnier, Paris méd. **11**:292, 1921.

R. Burnier quotes from the records thirty-one cases and adds two to the list in which mastitis of syphilitic origin developed during the secondary or tertiary phase of syphilis; in three cases the syphilis was inherited. Trauma was not incriminated in any instance. The swelling of the gland may occur with or without pain, and it often simulates cancer. The lesions generally subside in a few weeks whatever treatment is used, but in four of the cases several months elapsed before the conditions returned to normal. The assumption of a syphilitic origin should not be rejected too hastily. Only twenty of the total cases were in women, but there was no connection with a pregnancy except in one case.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, April 5, 1921

HOWARD FOX, M.D., *Chairman*

CHRONIC CIRCUMSCRIBED PAPULAR NEURODERMATITIS, INVOLVING THE AXILLAE, BREASTS AND PUBIC REGIONS.

Presented by DR. CLARK.

Miss H. Von L., 19 years of age, born in the United States, a stenographer, had a negative family history and her health was good. The trouble for which she was presented began eighteen months previously, when the patient first noticed severe itching in both axillae, which was soon followed by small firm, dry, conical, flesh-colored or pinkish papules that were intensely itchy. The number of papules slowly increased, with extension toward the trunk beyond the hairline. The papules were distinctly grouped, but showed no tendency to coalesce. Later, there was a distinct loss of hair, and the remaining hairs seemed dry, some of them being broken and stubbed. Two months ago, similar lesions appeared in a circular arrangement along the areola around both breasts, in a single row, and at the same time similar lesions developed along the upper margin of the hairs in the pubic region and the margins of the labia majora, and papules with macerated tops also appeared on the fourchette and inner surfaces of the labia majora. In the axillary region, the skin involved showed a succulent infiltration and thickening, with an exaggeration of the normal skin folds. None of the lesions had disappeared, and the itching had become intense, even excruciating.

The chemical analysis of the lood showed that it was normal; blood sugar, 90 mg. per 100 c.c.; urea, 5.1 mg. per 100 c.c.; uric acid, 1.07; creatinin, 1.01.

A biopsy showed a moderate acanthosis with lengthening of the epidermal pegs and a round-cell infiltration in the derma around dilated capillaries, together with some edema of the cells of the papillary processes of the derma. The deep sweat glands looked cystic, some containing granular material. There was a moderate round-cell infiltration around the hair follicles. As the groups of dilated sweat ascini seemed to lie beneath the hair follicles and the occluded ducts, this dilatation may have been due to involvement in an inflammatory process about the follicles.

DR. CLARK said that the case agreed in every particular with the two cases reported by Dr. George Henry Fox, with the exception that the lesions involved also the pubic region, the labia majora and the breasts. The itching was a serious feature of the case, and he asked for suggestions as to treatment.

DISCUSSION

DR. LANE agreed with the diagnosis, but said that it was rather unusual to have the condition so closely confined to the hairy region of the axilla. It

usually spread a little forward. He then asked whether roentgen-ray treatment had been employed, and, on being answered in the negative, said that that seemed to be the most promising treatment.

DR. HOWARD FOX said that the case corresponded closely with the ones his father had originally described and with a few that he had observed. He had that same day seen the eruption in a young woman who stated that her mother suffered from a similar condition. Both mother and daughter had had the disease since birth, but, unlike other patients with this disease, had never complained of itching. In another patient whom he had shown at a recent meeting, rapid improvement was being obtained with the use of roentgen rays.

CASE FOR DIAGNOSIS. Presented by DR. CLARK.

H. P., 38 years of age, born in Greece, was a clerk. His family history was negative and his general health had always been good. He had had syphilis in 1904, with a mild secondary eruption. For the past five or six years his fingers had been sensitive to cold and inclined to get purple during the winter months. Three months ago the middle finger of the left hand rather suddenly became violaceous in color, slightly swollen and somewhat numb. This condition had persisted, without much change except for a short period about a week ago, when the finger became swollen following an injury.

On examination, the whole finger was of a violaceous color, terminating in a sharply irregularly-shaped border at its base. The affected region presented a rather dry and shiny appearance, and in certain lights there appeared to be lichenification throughout the lesion. There was no infiltration of the skin, but the finger gave the impression of being slightly enlarged, and it was held stiff and straight. The fingernail was slightly chipped off, as were some of the other nails. There was a distinct tremor of the hand, and while the finger could be flexed naturally, there seemed to be some loss of muscle power in it, as well as a pronounced loss of power in the thumb and muscular atrophy between the thumb and first finger of that hand. The patient showed no distinct nerve disturbance other than a mild exaggeration of the deep reflexes and a diminution of superficial reflexes in various parts of the body.

The Wassermann reaction was negative, and radiographs of the finger showed no abnormality of the bony structure. The patient exhibited a few irregular and circular furfuraceous, scaly lesions on the upper area that looked like tinea versicolor. There had never been any pain or itching in any of the lesions.

DISCUSSION

DR. LANE inquired whether the patient had ever had any chronic paronychia, and on being answered in the negative said he had no diagnosis to offer.

DR. ABRAMOWITZ thought the possibility of a factitious eruption should be considered. The lesion did not conform to any other type of skin disease.

DR. CHARGIN inquired whether lupus erythematosus had been considered. There was some scaling suggesting that condition, and that possibility should be ruled out.

DR. LEVIN said that clinically the patient presented an acrocyanosis of the finger, and there was no scaling. He considered this condition a result of the application of a chemical, or some constriction at the base of the finger.

Dr. Wise said that the patient presented also scaly and circinate lesions on the right arm at its inner aspect, which were probably ringworm. The possibility of dermophytic infection of the hand should therefore be considered.

Dr. Gilmour remarked that he had noted a light erythematous lesion on the back of the hand which suggested the possibility of lupus erythematosus appearing later.

Dr. Kingsbury, referring to an inquiry that had been made about the fingernails, said that the man gave a history of trauma—the fingernail having been caught in a door—and stated that he had used numerous applications. The appearance suggested a phenol burn, and that possibility should be considered.

Dr. Clark added that the injury was sustained some time after the appearance of the lesion, and applications were made; after the inflammation subsided the appearance was about the same as before the injury.

Dr. Howard Fox said that the appearance of the finger suggested erysipeloid—a condition that was often due to handling crabs. This, however, was ruled out by the history and course of the disease. He was unable to make a diagnosis of the case.

Dr. Clark said he would have a biopsy made and would report on it later.

ATROPHIC FOLLICULITIS. Presented by Dr. Levin.

L. W., a married woman, aged 29, stated that she had had the black spots on the skin for two years. Scattered over the face, neck, trunk and extremities, there was a generalized condition of the skin characterized by the presence of pinpoint to pinhead sized and slightly larger black spots. These were not elevated but were level with the surface of the skin or were slightly depressed, and were situated in the mouths of the pilosebaceous follicles. These plugs could not be expressed, but after persisting for a variable period of time would fall out, leaving atrophic spots. The whole cutaneous surface except the palms was studded with the discrete black spots and atrophic lesions.

DISCUSSION

Dr. Wise said he had seen the patient when presented at another meeting. At that time, no definite diagnosis was made, but one of the speakers had suggested acne keratosa of Croker. That, however, was not accepted. The picture presented by the patient was unique in the experience of the speaker, and he was not aware of having read a description of a condition to fit the case.

Dr. Levin said that he had not known that the case had been presented before. He did not consider the condition to be acne, for there were no papules or pustules. He preferred calling it an atrophic folliculitis because it consisted essentially of a hyperkeratosis of the pilosebaceous follicles, with the subsequent dropping out of the plugs, leaving the lesions from pressure atrophy.

ERYTHEMA INDURATUM. Presented by Dr. Ochs.

R. L., a girl, aged 17, a stenographer, when first seen, early in February, presented a number of nodules in the skin of the outer aspect of the right leg. The arrangement of the nodules was more or less serpiginous in outline. Soon, however, they formed a nearly complete ring. The nodules were bluish red in color, were hard and painful to the touch and ulcerated; they would heal and ulcerate again. When the patient was first seen, the lesions resembled a serpiginous syphiloderma. The Wassermann test, however, was negative. In

spite of the negative Wassermann reaction, the patient received eight intravenous arsphenamin injections. Two or more Wassermann tests proved negative, and the lesions were not influenced by the treatment. A few days before presentation a new nodule appeared, somewhat larger than the old lesions, red, indurated and tender to the touch. This lesion was fairly typical of erythema induratum.

DR. OCHS supplemented the history by stating that the patient was the oldest child of eleven pregnancies, of which there were only three children living. The mother had had eight miscarriages, the terms being from four weeks to four months. The girl was apparently well until she was 15 years of age, when after a fall she had a little abrasion which ulcerated, and a few weeks later a series of small bumps or nodules appeared, shaped somewhat like a horseshoe. At first he had thought that the lesion was a syphilid.

DISCUSSION

DR. WISE said it was a difficult case to diagnose. He did not think it was syphilis. It might be the superficial sarcoid of Boeck, probably a benign miliary lupoid. It was not erythema induratum, for there was not enough infiltration in the depths of the tissue.

DR. LEVIN asked whether there had been any ulceration, and on receiving a reply in the affirmative, said that the fact that ulceration did not occur in the multiple benign sarcoid of Boeck would indicate that the case was not that type of sarcoid. He favored the diagnosis of erythema induratum.

DR. HOWARD FOX said that at first glance the eruption appeared to be a nodular syphilid. As this was excluded by the therapeutic test, he suggested the possibility of a sysosis, as there was a marked hypertrichosis of the leg.

KERATOMA SYPHILITICUM. Presented by DR. WISE.

F. T., 52 years of age, an American, single, a housekeeper, presented herself at the Vanderbilt clinic with a skin eruption on the plantar surface of both feet, which had been present for fifteen years. She admitted having had an initial lesion, followed by a secondary eruption twenty years ago. At that time the only form of treatment taken by the patient was pills, which had been taken for six months. When recently seen, she presented a verrucous mass interspersed with deep fissures, confined to the plantar aspect of both heels—the condition of the right was more serious than that of the left. The right heel had been involved for fifteen years and the left heel for two years. The Wassermann reaction was ++++.

DISCUSSION

DR. LANE said he had seen the patient two weeks before, and the condition had improved very much since that time.

DR. HOWARD FOX said that he, too, had seen the patient two weeks previously, and there appeared to be some improvement following the antisyphilitic treatment. The fact that the eruption was bilateral was, however, not in favor of a late syphilis.

LUPUS VULGARIS SIMULATING LUPUS ERYTHEMATOSUS. Presented by DR. LEVIN.

S. P., a man, aged 34, a native of Austria, had arrived in this country seven weeks prior to presentation. He stated that he had had the condition of the

skin for six months. On the left cheek there was an irregularly round patch the size of a half dollar. The center of the lesion was depressed and atrophic. The border was elevated and made up of pinhead-sized apple-jelly tubercles, which were very soft, as shown by compression with a toothpick. Scattered over the lesion were several characteristic tubercles. In the lower portion was an area which was white and scaly as the result of a trichloracetic acid application. On the right cheek was a smaller patch which was flat and scaly from acid applications.

DISCUSSION

DR. LANE agreed with the diagnosis.

DR. LEVIN said he had placed a question mark after the duration of the disease because he had discovered that the patient had received treatment abroad for years.

NEVUS UNIUS LATERIS. Presented by DR. LEVIN.

W. B., a schoolboy, aged 13, had had the condition of the skin since he was 5 months old. A small patch on the back of his neck had grown gradually and was followed by other patches on the neck, scalp and forehead. The skin on the middle of the forehead was covered by a linear elevated lesion with a verrucous surface covered with dirty grayish scales. The tip of the left ear was covered by a patch with similar characteristics. The left half of the neck showed similar linear lesions, extending from the scalp to the clavicle and forming rectangular and triangular figures with enclosed areas of normal skin. On the occipital region of the scalp was a flat, bald, white patch. Treatment had consisted of exposures to filtered and unfiltered roentgen rays, with good results—all the lesions were much flatter than when first seen, and the flat patch on the scalp had been the most elevated and warty.

DISCUSSION

DR. ROSTENBERG doubted the permanent effect of the roentgen rays and suggested that the lesions could be destroyed by fulguration. He then cited a case in which the same type of lesion was found, the size of a silver dollar, which was fulgurated four times and disappeared without leaving a scar. He was inclined to think that this method would be better in this case than the use of the roentgen rays.

DR. WISE said that it had been the experience at the Vanderbilt clinic that the result of roentgen-ray treatment was only a temporary disappearance of the keratosis, and that when the treatment ceased the keratosis was likely to disappear. He agreed with Dr. Rostenberg that the best treatment was either fulguration, the use of the actual cautery, or the curet.

CASE FOR DIAGNOSIS. Presented by DR. SCHEER.

G. B., a girl, aged 7 years, had been brought to Dr. Fordyce's clinic about ten days prior to presentation. At birth, the child's mother noticed a roughness of the lips, which gradually increased and was well marked when the patient was 1 year old. The mother also stated that the lesions varied in size—at times being very prominent, at other times barely noticeable. The lesions were limited to the mucous surface of the lips and adjoining buccal mucosa, and consisted of closely set nodules whose average diameter was one eighth of an inch; they were elevated from about one tenth to one eighth of an inch above the

surface of the lips. The color was that of normal mucous membrane, but when the lips were stretched the nodules appeared through the mucous membrane as yellowish-white bodies of firm consistence. On puncture no fluid contents could be obtained. There were no subjective symptoms. A biopsy was not permitted. The probable diagnosis was nevus.

Dr. Scheer said that he would like to have some suggestions as to treatment.

DISCUSSION

Dr. Lane suggested the diagnosis of lymphangioma.

Dr. Wise did not see any indications of angioma about the lesion. It might possibly be a lymphomatous nevus. The child showed a remarkable distortion of the teeth, and whether the same embryonic factor that caused the trouble with the teeth might not also have something to do with the lesions on the lip should be considered—for it undoubtedly appeared to be some form of nevus. When the lesions were palpated between the fingers they did not give the impression of a drop of water in the mucosa, but seemed rather more like sebaceous cysts.

NEUROTIC EXCORIATIONS. Presented by Dr. Bechet.

E. S., aged 47, from Dr. Trimble's service, stated that he had smoked opium extensively for eight years. For the past twelve or fifteen years this had been discontinued and morphia substituted. The latter drug was injected in the arms, an average of 60 grains a week being used. Seven months previously, while walking in the country, he was bitten very severely by "red bugs." Since that time, for no apparent reason, he had been in the habit of pinching the skin between the nails in order to get what he called "water" out. He stated that he frequently had to use all the strength in his fingers in order to expel this water. His wife had scabies and a positive Wassermann reaction. His Wassermann reaction was negative, and his disease antedated that of his wife. He presented for examination a considerable number of excoriated lesions, irregularly distributed in accessible parts of the body. The older lesions were pigmented; a few of the newer ones presented a bruised-like appearance.

DISCUSSION

Dr. Scheer said that the itching might have been caused by morphin. Morphin habitués frequently suffered from obstinate pruritus.

Dr. Bechet replied that the man did not complain of itching, but passed hours of his time in picking and pinching the skin. The patient was plainly neurotic, and in his estimation presented a typical picture of "picker's disease."

CASE FOR DIAGNOSIS. Presented by Dr. Wise.

A. S., 48 years of age, white, born in Russia, but living in the United States for five years, was a shoemaker by occupation. He presented himself at the Vanderbilt clinic with a generalized eruption of two years' duration. The face presented a dusky reddish-yellow appearance. The skin of the face was full of tumors and scales and gave a velvety feeling when touched. The upper edge gradually merged with the normal skin of the scalp. The entire skin from neck to knees presented diffused and irregularly outlined, faintly yellowish-brown plaques, free of scales, with extremely vague outlines, and a few areas of healthy skin between, distinctly resembling parapsoriasis en plaque. The lower

part of the legs, especially of the right, presented a series of plaques and tumors. The tumors varied in size from that of barley-corn grains above the right popliteal space to several inches in diameter on the calf. The right lower leg presented a widespread violaceous plaque which involved most of it. There was no definite anesthesia or marked enlargement of the ulnar nerves. The occipital nerves were not palpable. The patient's sexual power was not reduced. The buccal mucosa was not involved. The Wassermann reaction was negative, with alcoholic antigen and + with cholesterinized antigen. A biopsy was made on one of the tumors on the right lower leg, and Dr. Highman made a histologic diagnosis of leprosy. Lepra bacilli were seen in the section, confirming the histologic pitcure.

DISCUSSION

Dr. Abramowitz said he believed that the case was a nodular type of Hansen's disease.

Dr. Wise said that the man was a Russian, referred by Dr. Foerster of Milwaukee, and had lived in the United States for eighteen years. The reason they had hesitated about the diagnosis of leprosy was that no anesthesia was discovered by the usual routine tests, though it might be found by a careful neurologic examination. It might be interesting to the Section to know that Dr. Fordyce had diagnosed the case as leprosy only a few days before presentation.

Dr. Levin said that before accepting the diagnosis of leprosy the histopathology should be known and a search made for lepra bacilli in the tubercles. Other possibilities were parapsoriasis, mycosis fungoides, leukemia and sarcoma. Against the diagnosis of parapsoriasis were the presence of tubercles and the elevated, infiltrated, well-defined borders of the patches; against mycosis fungoides were the absence of itching and the color. A blood count and further investigation were necessary to rule out leukemia.

Last year Dr. Levin had presented a case of Kaposi's sarcoma showing tubercles resembling those on the leg in this case, and flat infiltrating patches, but with a more purplish color and not a russet as in this case. He leaned more to a diagnosis of Kaposi's sarcoma than to any other diagnosis.

Dr. Kingsbury thought that it was probably a case of leprosy, but that a diagnosis could not be made until determined by a biopsy.

Dr. Ochs agreed with Dr. Kingsbury.

DARIER'S DISEASE. Presented by Dr. Abramowitz.

Frank T., 24 years of age, American born and single, was referred to Dr. Fordyce's clinic by Dr. Thornley. His eruption started about two years previously while with the American Expeditionary Forces in France. He presented on the back and sides of the scalp isolated keratitic follicles the size of a pinhead. The entire interscapular region presented an inverted triangular area of used and isolated follicular keratoses. In addition, the extensor aspect of the arms and forearms showed a scattered follicular scaling. The diagnosis was confirmed by biopsy.

LICHEN NITIDUS. Presented by Dr. Parounagian.

Z. M., a Greek "bus boy," 19 years old and single, had been presented before the Section in October, 1920, and the case reported in the Archives of Dermatology and Syphilology in January, 1921. He had first noticed the lesions

about a year previously. When first presented, they consisted of minute shining papules, more pronounced on the flexor surfaces and most noticeable on the chest, back and genitals. There had never been any itching. The Wassermann reaction was + on Aug. 2, 1920, and was negative on Sept. 28, 1920. Between Aug. 2, 1920, and Jan. 13, 1921, he was given ten doses of arsphenamin in order to discover whether the skin condition would be influenced. On Feb. 15, 1921, his Wassermann reaction was again negative.

The lesions had improved remarkably since his first presentation.

In reply to an inquiry, Dr. Parounagian said that the patient had been kept under observation during the summer and given a placebo, and at last not knowing what to do, he was given arsphenamin in small doses, after which he improved gradually but steadily until he was almost entirely free of lesions.

DISCUSSION

DR. WISE said that the case was an interesting one. The man had had a distinct eruption of lichen nitidus when shown before. He understood that the condition had entirely disappeared as the result of treatment with arsphenamin. If that were true, it was most interesting, since pathologists generally considered the condition to be tuberculous in nature. The question was whether arsphenamin had actually caused the disappearance of the lesions on the shaft of the penis.

TERTIARY SYPHILIS. LEUKOPLAKIA. IODIN ERUPTION. Presented by DRS. PAROUNAGIAN and RULISON.

G. di. F., 41 years old, an Italian glovemaker, came to America eighteen years ago, and was under treatment at the Department of Syphiliolgy, Bellevue Hospital. He was married twenty-two years ago, and had no children.

Twenty-six years before he had had a chancre at the frenum, and was treated with injections of mercury at intervals for twelve or fourteen years. He stated that he had received over 100 injections. Fourteen years ago he developed a gluteal abscess or gumma, which he attributed to an infected needle. This abscess left a sinus, which persisted until his first treatment here, when it healed.

The patient complained of tremor of both legs, general pain and weakness and also of headaches and pain in the left eye.

His Wassermann reaction had been tested at Columbia Hospital on Jan. 14, 1921, and was found to be ++++. The Bellevue Hospital test of March 22, 1921, was also ++++.

The patient on admission presented a rash on the chest and back which was due to the ingestion of iodids. The medicine was discontinued and the rash disappeared. His inguinal and right epitrochlear glands were normal. He also had leukoplakia of the dorsum of the tongue, of both cheeks and an especially thickened pea-sized patch on the center of the lower lip.

He was given one dose of neo-arsphenamin on March 24, another on March 29 and a third on March 31.

FORDYCE'S DISEASE. Presented by DRS. PAROUNAGIAN and RULISON.

W. R., an American mechanic, 22 years of age, was admitted to the clinic at Bellevue Hospital in October, 1920, for treatment of secondary syphilis. At presentation, he had no syphilitic lesions, and his Wassermann reaction was

negative. He was presented on account of the xanthoma-like deposits under the mucous membrane of the upper lip. The patient stated that he did not know how long the lesions had existed.

DERMATITIS EXFOLIATIVA. Presented by DR. LEVIN.

L. K., a Russian, aged 62, a presser of cloaks, complained of a generalized pruritus of three weeks' duration. There was no history of a previously existing eruption. Four years prior to presentation, however, he had suffered from a similar condition of the skin, which disappeared after five weeks. Drugs had not been ingested. Constipation was severe. The skin showed a universal erythroderma with scaling. The erythema was brightest on the face, where there was a moderate edema. The exfoliation occurred in the form of fine scales, except on the palms and soles where the epidermis came away in large thick shreds. The underlying skin was smooth, red and shiny. There was no evidence of eczema, psoriasis or drug application. No signs or symptoms of leukemia or tuberculosis were found.

The blood showed a white blood cell count of 10,600, and the differential count was: polymorphonuclear cells, 78 per cent., and mononuclear cells, 22 per cent.; hemoglobin, 60 per cent.

LICHEN PLANUS AND POMPHOLYX OF THE HANDS. Presented by DR. LEVIN.

M. L., aged 52, a Russian by birth and a cloakmaker, was first seen about four weeks prior to presentation. At that time, he complained of itching and blisters of the hands, and showed numerous deep-seated pinhead to lentil-sized firm vesicles with serous contents. On his return to the clinic a week later, besides the vesicles on the hands, there was a papular eruption on the hands, wrists, penis and mucous membrane of the cheeks.

When presented, the palms showed deep-seated firm vesicles and torn vesicles with collarettes of epidermis. On the palms, dorsa of the hands, the wrists and glans penis, there were numerous polyhedral, umbilicated, shiny, scaly, violaceous, angular-based papules, varying in size from that of a pea to that of a pinpoint. Grouped papules were visible on the mucous membrane of the cheeks.

ZOSTERIFORM LICHEN PLANUS OF THE BODY. Presented by DR. ABRAMOWITZ.

Mrs. M. K., 48 years of age, American born, was from Dr. Fordyce's clinic. The eruption started about three months ago, appearing first on the tongue, which showed profuse pinhead-sized, pearly white plaques on its surface. The buccal mucosa also showed the typical pearly white streaks. Isolated and grouped violaceous papules were present on the wrists and flanks, the arrangement on the left flank being like that of an extensive zoster.

MULTIPLE SPECIFIC ARTHRITIS. Presented by DRS. PAROUNAGIAN and RULISON.

M. Q., an American saleswoman, 51 years old and single, was under treatment at the Department of Syphilology, Bellevue Hospital. No primary lesion had ever been noticed; secondary infections had occurred six years before. She took medicine by mouth for a few weeks, but ceased treatment as soon as her symptoms disappeared.

For about one year her right knee had been swollen. Six months ago her left knee was affected in the same way. Her Wassermann reaction was ++++ on Feb. 23, 1921. She was given six doses of silver arsphenamin and her general condition improved. The arthritis remained uninfluenced.

The reflexes were normal on admission. Both knee joints were swollen and painful on walking. The clinical diagnosis of Charcot's joint (early) was made.

The roentgen-ray diagnosis excluded Charcot's joint and classed the lesions as atrophic osteo-arthritis of both knee joints.

MULTIPLE ARTHRITIS. TERTIARY SYPHILIS. Presented by DRS. PAROUNAGIAN and RULISON.

M. W., from the Department of Syphilology at Bellevue Hospital, was a laundress, 44 years old, who was born in the British West Indies and had lived in America for twelve years. She was married at the age of 18, and her first two children were living and well. A third child was born alive, but died at the age of 2 weeks of "snuffles," and a fourth child was stillborn. A fifth pregnancy terminated normally, and the child was living and well. Her husband died fourteen years ago, after being ill for nine months with malarial fever.

The patient said that she had injured her left knee when she was a young girl and had had more or less trouble with it ever since. Six months ago she began to have joint pains involving both knees, both shoulders, the wrists and the ankles. The pains were much worse at night. There had been no swelling except that the left knee had always been swollen at intervals since childhood.

Her Wassermann reaction, taken at the Forty-Second Street Hospital before coming to Bellevue, was ++++. The blood test taken at Bellevue Hospital March 22, 1921, was negative. She complained of headaches, joint pains and stiffness. She had a marked Romberg sign; patellar and biceps reflexes were absent; she had sluggish triceps, and the pupils were equal and round and reacted sluggishly to light and accommodation. There was a slight haziness of the corneas.

The roentgenologic diagnosis was: "No evidence of abnormality of the distal half of the radius or ulna metacarpels. The outer half of the joint space of the right knee is increased in width. The articular surfaces are regular. There are hypertrophic, osteo-arthritic changes of the extremities of the femur and tibia. There is evidence of destruction of a portion of the inner condyle of the femur which suggests the presence of gouty tophi."

ANAL CHANCRE. Presented by DRS. PAROUNAGIAN and RULISON.

W. R., from the Department of Syphilology at Bellevue Hospital, was an American longshoreman, 26 years of age. He had lived with another longshoreman for a period of three weeks, beginning seven weeks ago. During this time, both men were drunk on several occasions. He denied any knowledge of abnormal sexual practices by his room-mate.

One month ago he noticed a slight itching and discomfort in the anal region. Seven days ago, the lower chain of inguinal glands began to swell. The upper inguinal glands of the left side were also moderately enlarged. Six days ago he developed a generalized maculopapular rash, generally distributed over the entire body. The throat was normal. The Wassermann reaction March 31, 1921, was ++++. Two dark-field examinations were negative. On April 5 a right inguinal gland ruptured.

The patient received two doses of silver arsphenamin: March 31, 0.15 gm., and April 4, 0.20 gm., and his condition was greatly improved.

IMPETIGO BULLOSA. Presented by Dr. Levin.

S. R., a girl, aged 2, presented a painful eruption of four weeks' duration. The lower half of the face, the hands and the diaper region were covered by large patches of denuded skin. Scattered over these areas were numerous bullous pustules as well as new pea-sized to pigeon-egg-sized bullae containing serous fluid, having flaccid walls, and situated on inflammatory bases. Several bullae had been torn and presented moist and crusted floors.

BROMODERMA TUBEROSUM. Presented by Dr. Ochs.

J. D., aged 14, born in the United States, was given triple bromids, 15 grains by mouth three times daily for four weeks, with the hope that it might relieve his stammering. When he came to the Lebanon dispensary six weeks ago he presented an ulceration the size of a hazelnut on his left shin and two smaller ones on the right shin. The ulcers appeared on a noninflammatory base and bore a close resemblance to syphilis. A Wassermann test was negative. Within a few days, however, the lesions began to vegetate and the mass rose one fourth of an inch above the surface. The vegetating mass soon broke down again and left behind a somewhat punched-out ulcer. The latter condition persisted to the time of presentation.

Paul E. Bechet, Secretary.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Stated Meeting, May 3, 1921

Howard Fox, M.D., *Chairman*

PROCAIN DERMATITIS. Presented by Dr. Highman.

In presenting this case, Dr. Highman stated that as a cutaneous condition it was of no interest; it was a dermatitis venenata. The patient was a physician who had used procain persistently for one year. The eruption was characteristic of nothing in particular except that it was keratotic rather than vesicular and highly pruritic.

A diagnosis of dermatitis from procain was made, and various skin tests were made to confirm the diagnosis. The test, when positive, did not seem to cause a wheal. After the substance was rubbed into the abrasion, there was at first a blanching anywhere from one-quarter to three-quarters inch around it, and from twelve to twenty-four hours later a patch of vesicular and itching dermatitis would develop.

Dr. Highman said that this was only the second time he had tried this reaction, though he had had three cases of this sort. Often in procain dermatitis there was an affection of the nails which caused the skin to peel back fanwise under the nail, producing a picture very much like tinea of the nails. The treatment was simple—the use of rubber gloves so that the procain would not come into contact with the skin for two or three weeks. Involution could be hastened by the use of roentgen rays if necessary.

DISCUSSION

DR. LÁPOWSKI said that he had had under his care many patients who were using different preparations, one of whom had been using dichloramin-T. The lesions appeared not only on the fingers but often patches of vesicles, sometimes of papulo-erythematous-desquamative form, were seen on the fingers, hands and face. The tests should not be applied to the affected arm but to some part of the body removed from the affected region in order to ascertain whether the same reaction would take place. The eruption could be made to disappear, but after using the objectionable preparation it would again reappear. It was not advisable to use the roentgen ray on any lesion which had a tendency to return.

DR. WILLIAMS said that it was a very interesting case. These eruptions of external origin were assuming more importance as they were recognized to be external dermatitis instead of eczema, as they were formerly called. It would be interesting to see what would happen if Dr. Highman would rub procain into the skin of a number of normal men. Such an experiment would show whether the skin of these patients had become sensitized to procain by constant handling of the drug.

DR. J. V. KLAUDER (Philadelphia) said that since the cutaneous tests had been in vogue their use had been extended not only in establishing sensitization to proteins but in determining the cause of dermatitis due to a variety of nonprotein substances. He had recently seen a physician who developed a dermatitis of the hands when in contact with arsphenamin or neo-arsphenamin. In this case a positive cutaneous test was obtained by the scarification method, employing a 1 per cent. solution of the drug.

DR. POLLITZER asked how far the condition was due to sensitization and how far the cutaneous tests were analogous to those in which there was a food product which had undergone changes in the digestive tract or in circulating blood. The tests seemed to be a demonstration of the sensitiveness of the skin to a particular poison and could not be called a cutaneous test any more than one could so designate rubbing poison-ivy leaf on a person who was sensitive to that poison. It was not analogous to a positive protein sensitization test, which implied an allergic state. In regard to the lesion itself, that was produced by the application to the scarified skin; the blanching of the skin was probably the effect of the epinephrin that was always put in these solutions. That point might be worth noting.

DR. ABRAMOWITZ, referring to the specificity of the procain skin reaction, said that Dr. Lane of New Haven had published some observations on this form of dermatitis in the March issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. In a dentist subject to this form of dermatitis, he obtained a positive skin reaction at the site of scarification and also in places where some of the test solution (procain) had accidentally been spilled. This, together with the cure of the dermatitis after protection against this drug, was convincing evidence of the specificity of the skin reaction.

DR. HIGHMAN said he did not think a test of this sort, employed with an inorganic matter like procain, indicated allergy in the restricted sense. The test was not made to prove an abstract scientific point, but it was obvious that some skins responded pathologically to certain drugs and others did not; the cause of the skin response was hypersusceptibility or susceptibility, or idiosyncrasy to a certain drug substance. If one suspected a certain drug of causing dermatitis, and by traumatizing the skin and rubbing in that substance

caused a similar eruption, an etiologic corroboration had been elicited; a test, within certain limits, had been established. He had tried this test in two cases, and in both the characteristic eruption was produced—not a wheal, that was purely traumatic—but an erythematopapular dermatitis. The test in this case had been made the previous day.

Dr. Highman said he had seen all the various phases of the disease which Dr. Lapowski described. He was misled by the first case, and thought it was tinea. This patient dropped the tablet in the palm of his right hand in making his solution, and just at that site a squamous lesion developed. As for regarding all dentists with dermatitis as having procain susceptibility, he had done so in one instance, but the patient declared he had never used procain. As a matter of fact that patient had used dichloramin-T.

CASE FOR DIAGNOSIS. Presented by Dr. Lapowski.

C. A., an Italian woman, aged 51, a houseworker, had been married for thirty-two years and had had eleven pregnancies; the first three children died in early infancy, two in babyhood, and six were living. The causes of death of the three were not known.

Thirty-nine years ago "erysipelas" developed on the patient's forehead, leaving a scar. Six months prior to presentation she had been operated on for removal of a uterine tumor.

The eruption presented appeared five years ago, beginning as a red spot near the left corner of the mouth and gradually spreading to the localization shown. The last patch appeared alongside the right eye six months ago. There was a sensation of itching and burning. The eruption consisted of (*a*) miliary papules, (*b*) larger papulotubercles, and (*c*) a large plaque, slightly infiltrated and sharply defined, occupying the region of the chin and lower portion of the cheek. The papulotubercles were arranged in annular and semi-annular form, some of them conglomerated in one patch (above the external corner of the right eye and lower edge of the right jaw) which was soft, erythematous, and on diascopic pressure presented a brownish pigmentation with deep miliary points scattered and in bunches. Above the right eye was a longitudinal scar, white and slightly deeper than the surface of the skin. The origin and age of the scar could not be ascertained. The whole face and part of the forehead were occupied with the papulotubercles, which were soft to the touch—some of them dark brown, some of them pale and raised above the skin and covered with thin scales. On the anterior surface of the neck were scattered papulotubercles, some arranged in large annular formations, some disseminated. There were no ulcerations. There was a slight pruritus, but no marks of scratching.

The patient came to the clinic twenty-four hours prior to presentation, and no detailed examination had been undertaken.

On the first aspect in daylight, the lesions looked like papulotubercular syphilid, but owing to the persistence of the same lesions without undergoing any changes during five years, the likely diagnosis of syphilis was abandoned.

Dr. Lapowski suggested the diagnosis of benign multiple sarcoid of Boeck.

DISCUSSION

Dr. Wise offered a tentative diagnosis of pseudoxanthoma elasticum, on account of the apparent translucency of some of the lesions as seen by poor artificial illumination.

DR. POLLITZER said that it was impossible to make a diagnosis without further data, and that nothing was to be gained by guessing.

DR. HIGHMAN said he had nothing to add except to protect his impression that the case might be in that wide group of which so little was known, the lymphoderma group, that is, pseudoleukemia or mycosis, etc. The woman had said something about itching, but since she spoke only Italian it was difficult to understand her. Whereas in most itching dermatoses one saw scratching effects, often in cases of pseudoleukemia and mycosis with itching he had not noticed them. The color and the type of infiltration made it seem probable that the condition was one of the lymphodermas. He agreed with Dr. Pollitzer, however, that any diagnosis at present was largely a matter of guesswork.

DR. WILLIAMS directed attention to one symptom that had not been mentioned—there were distinctly palpable masses above the internal condyle of each elbow. These might be enlarged epitrochlear glands, which would accord with a diagnosis of leukemia; or they might be enlargements of the ulnar nerve, which would accord with a diagnosis of leprosy. It was certainly true that one could not make a diagnosis in such a case without a biopsy, but the more that could be gained by clinical observation the better.

DR. LAPOWSKI said that what Dr. Williams had suggested about the swelling nerve trunk in the elbow region had been noted by one of the physicians who suggested the possibility of leprosy. He emphasized the presence of the miliary brownish points when pressed with a diascope to support his diagnosis of benign multiple sarcoid. Further, he said he could not agree with the suggestion of Dr. Pollitzer that one was not able to make a tentative diagnosis without further examination, since dermatologists should endeavor to arrive at a diagnosis of a case from the clinical facts—from the aspect and cause of the lesions—and only have recourse to other methods in support of the clinical findings.

URTICARIA PIGMENTOSA IN AN ADULT. Presented by DR. HOWARD FOX.

I. S., 37 years old, was a married woman, born in Russia. Her menses were established at the age of 13 and had always been regular. She was the mother of two apparently healthy children. She had had a half dozen miscarriages, most of them about the third month. Two years ago she gave birth to a dead child at full term. With the exception of severe chronic constipation, she had always enjoyed good health. She complained of considerable annoyance from a sensation of burning or itching, not severe enough to produce excoriations. She denied any knowledge of infection with venereal disease.

The eruption first appeared about ten years previously and had gradually increased up to the present time. It consisted of a large number of discrete pinhead to pea-sized macules of a yellowish brownish color. They were situated on the neck, upper third of the back, outer aspect of the arms and backs of the hands, the flexors of the forearms, buttocks, and antero-internal aspect of the thighs. The palms were free. The patient stated that none of the lesions, to her knowledge, had ever disappeared. They became markedly urticarial on friction, a fact of which the patient was well aware. She was a woman of medium height, weighing 156 pounds. The result of the biopsy and Wassermann reaction had not been reported.

DISCUSSION

DR. HIGHMAN did not think the patient had urticaria pigmentosa. The condition was more like what the French described as papular urticaria with pigmentation, which was probably a different clinical entity. One could not make a diagnosis of urticaria pigmentosa in such a case without finding mast cells at some stage in the development of the papule. As Hartzell had mentioned, in the stage of involution even typical urticaria pigmentosa might not show mast cells, and unless one could submit a slide in this case of a developing papule showing mast cells he did not think one could accept the adult case as urticaria pigmentosa. He suggested this as a caution in formulating concepts of dermatoses of this variety.

DR. LAPOWSKI said that one might call the condition urticaria with pigmentations, for that was a passing form. He had known this patient for six years, during which time she had exhibited the same lesions. In collecting with care the past histories of such patients, one usually obtained corroborations in the forms of past outbreaks of urticaria and itching to support the diagnosis of urticaria pigmentosa.

DR. WISE said that Dr. Highman's remarks were very pertinent, but he believed that cases of urticaria pigmentosa beginning in adult life are now and then encountered, exhibiting mast cells on section.

DERMATITIS HERPETIFORMIS. Presented by DR. LAPOWSKI.

L. L., 35 years of age, and married, was born in Russia and was a housework er. Both her family and past history were negative. The first attack occurred three years previously on the body and face; the second attack occurred one year previously, two years after the first one, with severer manifestations than the first attack, larger bullae and vesicles covering nearly the entire body, accompanied by severe itching. She entered Mount Sinai Hospital where she was treated with one intravenous and several intramuscular injections of what was probably arsenic. The eruption disappeared.

Six months ago she came to the dispensary with a third attack, showing (1) scattered scratched papulotubercles on the face, shoulders, buttocks and thighs, symmetrically arranged; (2) on the trunk, especially around the sacral region and back, were pigmented areas, surrounding patches of skin in which were visible many pea-sized scars. The mucous membranes were free.

She was treated with injections of neo-arsphenamin and mercuric chlorid. During the course of the treatment, large bullae appeared on the palms and soles, symmetrically arranged, and papulotubercles over various portions of the body.

HYDROA AESTIVALE. Presented by DR. WISE.

S. G., a boy aged 7, born in the United States and in good general health, presented himself at the Vanderbilt clinic with an eruption which consisted of a few deep-seated isolated vesicles of two weeks' duration, confined to the ears. These lesions were pruritic. This was the patient's second attack. The first attack occurred last spring and persisted until the fall.

DISCUSSION

DR. BECHET did not doubt the correctness of the tentative diagnosis. He had recently observed a frank case of hydroa vacciniforme at the Bellevue

clinic, in which the patient had typical lesions on the face and varioliform scarring from previous outbreaks. The active lesions on the ears in his case were exactly similar to those in Dr. Wise's case.

EPIDERMOLYSIS BULLOSA. Presented by DR. GILMOUR.

J. B., an Italian, 23 years old and married, had a negative family history. Since the age of 3, blisters had appeared on the hands and feet. Those on the feet appeared only in the summer (May to September, inclusive). The blisters often came on the hands, and there was a definite history of trauma noted. One-half hour of ironing a week previously caused several blisters to appear on the right hand. These were out of proportion to the pressure exerted. Blisters had not appeared on the backs of the hands or other exposed places. No scarring or pigmentation had been left. On the day of presentation, small blisters appeared without apparent cause on the palmar surface of the right little finger. For the past three days blisters had been present on the bottom of the big toe and the one next to it. The diameter as presented was three-quarters inch. An associated keratosis pilaris of the limbs was present.

DISCUSSION

DR. HIGHMAN asked whether Dr. Williams did not consider this a case of epidermophytosis or tinea.

DR. WILLIAMS replied that he thought it was not, for the reason that blisters which occur in tinea of the toes or hands were generally deep, not superficial; instead of rupturing easily, they ruptured with great difficulty in the early stages. These, on the other hand, were superficial, such as seen in epidermolysis or pemphigus. The vesicles of tinea were almost always small, and any large ones were formed by confluence of many small ones. He would rule out tinea in this case.

DR. WISE did not think the case was epidermolysis bullosa because of the lack of the little epidermal cysts which every case showed. He would like to have some one familiar with French literature express an opinion as to the diagnosis of acrodermatitis hiemalis in this patient.

DR. GILMOUR said that against the diagnosis of epidermophytosis was the fact that the blisters came out suddenly. One had appeared on the finger that day. None of those on the feet were over three days old, and some were less than that. He asked for suggestions as to treatment. No pigmentation or scarring was present.

UNIVERSAL ALOPECIA. Presented by DR. GILMOUR.

P. S., an Italian, aged 35, married, a moulder, was the father of a child with a similar condition, presented at the same time.

For a period extending over three months there had been a gradual loss of hair, which became total. This began nine years ago, and since that time there had been a complete loss of hair.

ALOPECIA AREATA. Presented by DR. GILMOUR.

G. S., a schoolboy, 8 years of age, was the son of the preceding patient. There had been a complete alopecia of the scalp for one year. The lashes on the right eyelid had been absent for nine months; those of the left eyelid were still present.

SPOROTRICHOSIS. Presented by Dr. Wise.

K. S., aged 33, an Armenian by birth, had been in the United States only a few months, and had been working as a brass polisher. He presented himself at the Vanderbilt clinic with a dime-sized papular lesion of two months' duration on the dorsum of the right hand. The lesion was ulcerated at the center and was surrounded by a wide area of erythema. There were also numerous pea-sized subcutaneous nodules, extending from the wrist to the shoulder. These nodules were rather hard and showed no signs of breaking down. The lesion on the dorsum of the hand began as a small pea-sized papule which grew larger, unattended by pain. Cultures and a biopsy were taken, but the results had not yet been reported.

DISCUSSION

Dr. Highman said that the case was probably sporotrichosis, though it might possibly be blastomycosis.

GRANULOMA ANNULARE. Presented by Dr. Williams.

M. C., a man aged 23, about one year previously had a small flat papule at the base of the first finger of the left hand, which was quickly followed by the appearance of about twelve others in the immediate vicinity, the entire group occupying an area of about 1½ inches in diameter. At the same time, a single lesion appeared on the back of the right hand, also at the base of the first finger. The individual lesions were soft, circular, discrete, yellowish-pink in color; some were distinctly annular with a depressed center, while others had only a slight umbilication in the center. There was no itching and the lesions had not spread, and they had grown little, if at all, since their first appearance.

LICHEN PLANUS. Presented by Dr. Williams.

G. K., in August, 1920, had had a lesion on his upper lip, which he described as a cold sore, but which did not crust over as an ordinary cold sore would and which persisted for a long time. In about one month, a similar lesion appeared on the lower lip. As time went on, the lesions became less elevated and were rather flat, the lips having the appearance of being chapped. There was slight itching. The condition was treated at various clinics, and the patient was shown before several society meetings where the diagnosis was considered to be either lichen planus or lupus erythematosus. The patient was treated with sodium arsenate internally and salicylic acid salve externally, with no improvement. He stated that under roentgen-ray treatment there was a marked temporary improvement, but this soon relapsed while the roentgen-ray treatment was still being given. About a month ago several small papular lesions appeared on the backs of both hands and one on the penis. These lesions were discrete flat-topped papules with abrupt sides, rather circular in shape and bluish pink in color. The lesion on the penis was of the same nature, and there was little or no itching.

FRAMBESIFORM SYPHILID. Presented by Dr. Williams.

G. D., 36 years old, was a butcher on the sea, sailing between New York and Hamburg. He had not been in the tropics. Eight weeks ago, while being shaved in a barber shop, he was cut by the barber. He later noticed three

small growths appearing on his chin. These growths rapidly attained the size exhibited and then remained stationary. Three months ago, or about five weeks prior to the appearance of the lesions, the patient had a sore on the penis, which was diagnosed as herpes. It was treated with dusting powder and disappeared in about two weeks, leaving a small scar. When presented, the patient had one large lesion below the left corner of his mouth, which was about three-eighths inch in diameter and consisted of a raised verrucous patch which two weeks before was covered with a slight crust. There were two or three similar but smaller lesions in the vicinity. There were several small scratched lesions on the scalp.

The treatment had consisted of boric acid ointment and two injections of silver arsphenamin, one a week ago, and a second on the day of presentation. The Wassermann reaction was ++++.

Dr. Williams said that the man first came to the hospital two weeks previously and presented then the picture shown tonight, except that the lesions were more elevated and warty. The lesion on the left angle of the mouth was covered with exudation and had very much the appearance of blastomycosis or tuberculosis verrucosa; it was not like the ordinary syphilid—but the man had a ++++ Wassermann reaction and a history of chancre; he also had a small pustule on the scalp, which Dr. Lapowski claimed was characteristic. In Crocker's textbook a similar case was described, the patient having a few lesions on the face and a chancre a few months later, with other eruptions on the body. Ehrlich's diagnostic atlas contained a colored plate showing almost the same lesion on the cheek. Several of the men who had just seen this case said that if the man had been seen in the tropics a diagnosis of yaws would have been made. J. Hutchinson reported a case of a man from Ceylon who contracted syphilis in London and presented a secondary eruption like yaws. This case seemed to be a secondary syphilid. Some of the textbooks did not mention it; others said it was uncommon.

DISCUSSION

Dr. Klauder (Philadelphia) said that it was difficult on purely clinical evidence to differentiate yaws from a frambesiform syphilid. The lesions in this case bore a close resemblance to yaws; on the other hand, one could not gainsay the diagnosis of syphilis. Further study would be necessary in order to establish the diagnosis, and he believed that such study would show the case to be yaws. The laboratory diagnosis between yaws and syphilis was not easy. The diagnosis could not be made with certainty by the Wassermann reaction, although this reaction performed with an extract of yaws' nodule as an antigen might be of help in differential diagnosis. In a recent study of a case of yaws, by Dr. Schamberg and himself, morphologic differences between *Spirochaeta pertenuis* and *Spirochaeta pallida* were observed in stained specimens, although under the dark field these organisms were undistinguishable. The differential diagnosis was difficult to make by rabbit inoculations of the two organisms. The lesions of both yaws and syphilis disappeared after the administration of arsphenamin; hence the diagnosis could not be made in this manner. If the Wassermann reaction became negative after a few injections of arsphenamin, the diagnosis of yaws was favored, whereas in syphilis it was likely that many more injections would be required to make the Wassermann reaction negative. The only satisfactory way of making a laboratory diagnosis between yaws and syphilis was by a crossed inoculation of a monkey's eyebrow. If the spirochetes obtained from this case

were inoculated in one eyebrow of a monkey and after a positive result was obtained the other eyebrow was inoculated with spirochetes known to be pallida, a positive result would make the diagnosis of yaws. In other words, monkeys infected with yaws did not become immune to syphilis. On the other hand, a successful inoculation of a monkey's eyebrow with syphilis precluded obtaining a second successful inoculation with syphilis soon after the first one.

DR. HIGHMAN said that Dr. Klauder's points were well taken. Yaws seldom started except on exposed areas. In this case, the primary sore had been penile, favoring syphilis. Microscopically, in syphilis the parasites were prevailingly found deep; in yaws, in the epiderm; while in yaws even more plasma cells were found than in syphilis. These data, together with the fact that after all syphilis might clinically look like this, though rarely, substantiated Dr. Williams' interpretation of the case.

DERMATITIS MEDICAMENTOSA — PHENOLPHTHALEIN. Presented by DR. CHARGIN.

Y. R., 58 years of age, married and a laborer, had a history which dated back six weeks, at which time there appeared an eruption scattered over the body, following the ingestion of four tablets of "Rexall's Orderlies," a preparation containing 1 grain of phenolphthalein per tablet. The onset was sudden, and the eruption was round, erythemato-pigmented—the individual lesions varying in size from that of a ten-cent piece to areas larger than a silver dollar. On ceasing the use of the drug the eruption involuted, leaving, however, pigmented circular areas—the pigmentation being more marked at the center than at the periphery of the individual lesions. Resumption of the remedy, even a single tablet, resulted in the recurrence of the original lesions and the appearance of new ones. At the time of presentation the patient showed the erythemato-pigmented areas in the various stages of involution. The eruption was to be noted on the forehead and neck, at the hair margins, the concha of left ear, anterior aspects of the arms, back of the chest, abdomen, sacral region, buttocks, genito-crural region and outer part of the legs.

DERMATITIS MEDICAMENTOSA (ARSPHENAMIN). Presented by DR. CHARGIN.

M. M., 34 years of age, married, and a clothing presser was the subject of cerebrospinal syphilis and had been under treatment for several years. In the course of treatment, in addition to mercury, he had received twenty-seven arsphenamin injections. With the exception of an occasional secondary reaction, the patient experienced no ill effects from the arsphenamin administrations. Beginning with the twentieth and following subsequent injections he had been developing a fixed erythemato-pigmented eruption, limited to the right cheek and upper aspect of the left thigh. The lesion of the cheek covered an area larger than a silver dollar, whereas the patch on the thigh was the size of a ten-cent piece. There were no other lesions. Following each injection of arsphenamin after about five to six hours, the original erythematous areas lighted up again, and in the course of time the erythema gradually disappeared leaving pigmented areas similar in all respects to a mild phenolphthalein eruption. This was the second case of this type that had come under Dr. Chargin's observation, the first one having been reported in the *Journal of Cutaneous Diseases* **37**:622, 1919.

XANTHELASMOIDEA. Presented by DR. GILMOUR.

M. L., aged 3½ years, born in the United States, at the age of 3 months had a red macular rash on the abdomen. This gradually spread and covered the entire trunk and limbs. The face remained free. The rash gradually became darker. Itching occurred only in hot weather. There was no eruption of the nodular type.

PAPULONECROTIC TUBERCULID. Presented by DR. OCHS.

Mrs. M. W., 33 years old, born in Hungary, had suffered from an eruption for the past nine years, at no time being free from the disease. It consisted of both superficial and discrete papulopustules which were elevated and eventually left scars. The color varied from a slight pink to a deep red. Active lesions and scars were most numerous on the legs, a few being present on the arms, chest and upper part of the back. They occasioned no subjective symptoms. The diagnosis of a papulonecrotic tuberculid had been confirmed by a biopsy. The Wasserrmann reaction was negative. The patient was also suffering from a marked polycythemia (Vaquez' disease). The hemoglobin varied at different times from 120 to 158 per cent., and the red cells from 9,500.000 to 10,900,000. The white cell count was 10,200.

DISCUSSION

DR. POLLITZER expressed some doubt as to whether the condition was a papulonecrotic tuberculid and suggested that it might be a papular prurigo-leukemia. The blood count, of course, was peculiar but might more or less fit in with a leukemic disturbance. The red blood count was tremendously high, and one suspected that something was wrong when it was stated that 10,000,000 red blood cells were counted in blood from the finger tip and 7,500,000 in blood taken from another point at the same time; certainly the circulating blood did not differ so greatly in different parts of the body. The white blood cells could not be regarded as increased in view of the polycythemia. It was unfortunate that no differential count had been made.

DR. LAPOWSKI said that clinically the case did not look like a tuberculid. The lesions on the arm resembled more a pruriginous papule, and the erythemato-urticarial patch on the chest, with itching, would support Dr. Pollitzer's suggestion.

DR. WISE said he had had an opportunity to examine the slide and it looked like a tuberculid, not a granuloma. Histologically, the diagnosis of tuberculid was more likely than prurigo. Whether or not there was any relation between a tuberculid and polycythemia was to be considered, but his impression was that the skin disease and the polycythemia were not related, and that the patient had two conditions. So far as he could remember, the slide showed an inflammatory reaction in the corium, evidences of necrosis, with ordinary inflammatory cellular exudates so commonly seen in biopsies of papulonecrotic tuberculids.

DR. HIGHMAN, referring to Dr. Wise's remarks, said that the histologic report was not enough to base a diagnosis of tuberculid on. To begin with, we are still confused as to the standard morphology of tuberculids. They show various pictures. One cannot make a diagnosis of tuberculid histologically unless something suggesting tuberculosis is seen. The fact that nothing but lymphocytes were seen would not indicate tuberculid more than leukemia or pseudoleukemia.

Dr. Howard Fox said that the intense itching of which Dr. Ochs had spoken would be an indication against the diagnosis of papulonecrotic tuberculid.

GRANULOMA INGUINALE. Presented by Dr. Rosen.

J. H., a mulatto, 23 years of age, a porter, born in the United States, presented a deep, crusted, sharply bordered ulcer in the right inguinal region, measuring 2½ by 1½ inches. It had existed for two years. No *Spirochaeta pallida*, but numerous other spirochetes, had been found. A biopsy and culture were made, the results of which will be reported later.

DISCUSSION

Dr. Klauder said he did not think there was any doubt as to the diagnosis, since he thought the lesions were typical of granuloma inguinale. The finding of spirochetes on the surface of the lesions should not complicate matters, since it was not remarkable to find a variety of spirochetes on any ulcerating surface.

Dr. Williams agreed with the diagnosis.

Dr. Wise regretted that Dr. Klauder's diagnosis was not confirmed microscopically. Dr. Teague, who examined the lesion bacteriologically, was unable to find Leishmann-Donovan organisms in the scrapings and tissues, nor were tubercle bacilli discovered.

Dr. Herman Goodman said that he had been able to demonstrate the causative organism in three out of four cases seen in the tropics. The method he had found to yield the best results was that of using tissue smears. The surface of the lesion was cleansed and a portion of the active margin removed. The portion cut was then trimmed so that only deep tissue was available. This was washed in saline, expressed, and smears were made. In this manner, no superficial contaminating organisms were present to cause confusion.

After he had advised this procedure, the organisms had been demonstrated in a patient on Dr. Clifton's service at the New York Skin and Cancer Hospital. Only that afternoon he had carried out the procedure on a patient on Dr. Parounagian's service at Bellevue Hospital, and the organisms were demonstrated. Previous examinations of tissue and smears had not been successful.

There had been some difference of opinion as to the bacterial agent of the condition. There had been confirmatory evidence accumulating for the two main contenders, namely, for the Calimato-bacterium granulomatis origin, and this was the organism demonstrated in the three hospital cases under his observation, and the spirochete aboriginalis origin. This organism was demonstrated in the fourth of his cases. It was certain that this spirochete was neither the *S. pallida* nor the *S. refringens*.

In four other tropical cases that he had seen but not studied intensively, the organisms had not been demonstrated.

He had made bacteriologic studies of tissue from the patient presented at the December, 1920, meeting of the Section (*Arch. Dermat. & Syph.* **3**:331, 1920). Dr. Stein had been kind enough to furnish this material at operation, but he had not succeeded in demonstrating the organisms in that case.

Paul E. Bechet, Secretary.

SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MADRID

Regular Meeting, May 4, 1921

DR. AZÚA, *Presiding*

SILVER ARSPHENAMIN AND MALTA FEVER. DR. BERTOLOTY.

Dr. Bertoloty had two patients with Malta fever who had been treated with all the usual measures without any success. He tried silver arsphenamin with such good results that he considered it his duty to report the fact to the society, since the cure was complete.

DISCUSSION

DR. SAINZ DE AJA added to the two cases Dr. Bertoloty reported, one more in which arsphenamin had been used. After the first injection the fever cycle disappeared; then recidivation occurred. More arsphenamin was administered, and the patient recovered completely.

SERPIGINOUS ULCER. Presented by DR. COVISA.

The patient had already been presented in previous sessions. As no relief was obtained with local treatment, Dr. Covisa recalling Criado's patient who recovered after tuberculin treatment, applied this agent. After the first injections she improved remarkably. The treatment was stopped, and the patient grew worse. Tuberculin was tried again, and now the patient is almost entirely well. Two patients with cases of the same nature have therefore been cured; this seems to be important.

DR. CRIADO did not consider this a mere coincidence. He recalled that in his case the serpiginous lesion healed before the tuberculous gummae.

DR. SAINZ DE AJA said he was interested in knowing why these patients recovered after tuberculin treatment. In his opinion, there occurred a tuberculinization of the lesions which might suggest why they became serpiginous-venereal on the surface and tuberculous at the bottom.

DR. AZÚA said that it was not known what serpigo was. Therefore it might be considered venereal in origin without being so. He mentioned six cases in which great improvement was noted in the patient after the administration of potassium iodid. Apparently the presence of Ducrey's bacillus is not necessary in a serpiginous lesion. Dr. Azúa thought that in the two cases of Criado and Covisa a definite cure had been obtained with tuberculin by chance, and that the lesions were tuberculous lesions of atypical forms.

DR. COVISA considered the problem more complicated because there are doubts as to whether tuberculous lesions are cured by tuberculin and because serpiginous zones were healed before the tuberculous ones.

CASES FOR DIAGNOSIS. Presented by DR. SAINZ DE AJA.

Two patients had almost identical ulcerated lesions of the phagedenic type, which had nearly destroyed the foreskin and had pushed their way 2 cm. below the pubic skin. In both, specific treatment had failed. Since these may be cases of venereal serpigo on a chancre base they will be treated with tartar emetic. The patients were presented so that they might be examined before treatment.

ALOPECIA AREATA AND SYPHILIS. Dr. Sanz de Grado.

Several cases of pelade are reported in which a careful examination disclosed syphilis. Therefore Dr. Sanz de Grado thought that in view of the theories of the French school a like investigation must be made of all patients with pelade.

Dr. Sainz de Aja said he had discussed on another occasion the lack of relationship between pelade and syphilis. In the cases in which he had seen this association, pelade patches had never healed with specific treatment.

Dr. Covisa stated he had not seen a relationship between both conditions but out of regard for Sabouraud's views it should be either confirmed or disproved.

Dr. Gimeno agreed with Dr. Sainz de Aja, saying he had looked for syphilis in his patients, and in most of them he could not find it.

Dr. Azúa did not believe that there was any relationship between alopecia areata and syphilis, as he had stated six years ago. This does not imply that Dr. Sanz de Grado has not reported his cases properly, and the repeated therapeutic successes justify consideration of this relation.

ONYCHOTRICHOPHYTIA. Presented by Dr. Grande de Riego.

This clinical case had been confirmed by laboratory examination, and as roentgen-ray treatment had failed, the patient will be treated with vaccines.

VARICOSE ULCER TREATED BY INTRAVENOUS INJECTIONS OF SODIUM CARBONATE. Dr. Forns.

A patient from Dr. Aja's service in San Juan de Dios Hospital had had varices in both legs for fifteen years, presenting multiple ulcers which healed and reulcerated frequently. When the patient was first observed she had had, for a long time, a superficial ulcer in the lower third internal aspect of the left leg about the size of a dollar. She was treated according to Sicard's method with injections of 5, 7, 9 and 10 c.c. The ulcer disappeared at the fourth injection, and the patient was dismissed at the end of fifteen days. The only local treatments were hot packs of permanganate.

Dr. Barrio de Medina, Secretary.

TWELFTH CONGRESS OF THE GERMAN DERMATOLOGICAL SOCIETY

May 15-19, 1921

A congress of about 400 specialists in skin and venereal diseases was held in Hamburg. Besides Germany, Austria, Sweden, Norway, Holland, Denmark, Finland, Czecho-Slovakia, Japan and Spain were represented.

SYPHILIS AND THE SPINAL FLUID. Professor Nonne.

Professor Nonne, the neurologist, was the first speaker. Basing his statements on fifteen years of experience, he emphasizes the necessity of making diagnosis, prognosis and treatment of pathologic spinal fluid depend on the exact control of (*a*) the number and species of cells, (*b*) spinal fluid pressure,

and (*c*) globulin reaction. There is generally a slight rise in spinal fluid pressure in tabes and progressive paralysis. A distinct rise is seen in syphilitic meningitis. As to lymphocytosis, 40 per cent. of all syphilitic patients show an increase of lymphocytes without showing any nerve symptoms. Nonne then pointed out differences in the development and course of tabes and progressive paralysis. He stated that progressive paralysis in exceptional cases can be cured (mentioning six of his own patients). The missing globulin reaction is the proof that cure has been effected—as the globulin reaction is seen only in true syphilitics. The Wassermann reaction was then mentioned. This is positive in all cases of tabes and progressive paralysis—generally showing a stronger reaction in the latter. A positive Wassermann reaction is not in itself an indication for treatment. Several cases were mentioned and examples given to demonstrate this. Hemolysin reaction is not considered specific for syphilis by Nonne, although this reaction is seen in both tabes and progressive paralysis. In some cases the nervous system is attacked by syphilis as early as a few months after infection. The cerebrospinal fluid, as a rule, soon becomes infectious. In spite of this, 60 per cent. of patients with primary and secondary cases of syphilis with pathologic fluid are cured. Normal cerebrospinal fluid does not prove the absence of syphilis. The speaker again emphasized the necessity of examining the cerebrospinal fluid in cases of isolated Argyll Robertson pupil in syphilitic meningitis for exact diagnoses. As to the effect of treatment on cerebrospinal fluid, good results are obtained contrary to the experience in progressive paralysis, in which the effect is only transitory. In spite of this, clinical symptoms may show rapid movement. The success of treatment will always depend mainly on the degree of infection and the strength of the defensive action of the system. In summarizing, Nonne cautions against treating diseases instead of patients, against trying reactions instead of considering the state of health of the infected person.

SYPHILIS AND THE SPINAL FLUID. Dr. Kyrle.

Dr. Kyrle of Vienna said that soon after infection the cerebrospinal fluid may become pathologic. He did not believe that skin symptoms, that is, a projection of the disease into the skin, protect the spinal fluid from infection in any way. In leukoderma and alopecia specifica the speaker had often seen positive spinal fluid tests. Normal spinal fluid at the beginning of the secondary stage means little. Beyond the second year after infection, however, the spinal fluid rarely becomes positive. As for treatment, Kyrle recommends mercury and arsphenamin, especially the latter. Insufficient cures with arsphnamin are apt to cause provocation.

MERCURY COMPARED WITH ARSPHENAMIN. Dr. Kolle.

Dr. Kolle of Frankfurt described his experiments on rabbits with the numerous solutions of mercury now on the German market as compared with arsphenamin. He failed to cure the syphilis of rabbits, contrary to the experience with arsphenamin.

ABORTIVE TREATMENT OF SYPHILIS. Dr. Rost.

Dr. Rost of Freiburg mentioned 882 cases of seronegative syphilis. In 736 of these there were no relapses after one year, in 305 no relapses after from one to two years, and in 319 no relapses after two years. No definite standard method of treatment was agreed on, yet on the whole the combined treatment was preferred and seemed to dominate.

RELATION OF DERMATOSES TO INTERNAL SECRETION. Dr. Brock.

Dr. Brock of Kiel pointed out the relation of dermatoses to internal secretion. He believes in the influence of the thymus gland on psoriasis. The therapeutic measures resulting herefrom (stimulating doses of roentgen rays) are a new factor in the treatment of psoriasis. Other diseases, such as lichen ruber planus, ichthyosis and ichthyosis hystrix were well influenced by this method.

METHOD OF APPLYING TURPENTINE. Dr. Klingmüller.

Dr. Klingmüller of Kiel explained his method of applying turpentine. A 10 per cent. solution is given into the gluteal region in varying doses from 0.5 to 5 c.c. Klingmüller could not explain how this agent acts—he does not think that a direct influence on lesions thus treated is possible.

INJECTIONS WITH MILK. Dr. Müller.

Dr. Müller of Vienna, speaking of injections with milk, said that the greatest effect of these injections was obtained in transudation and hyperemia. He thinks the stronger inflammation is caused by the changes in the colloidal balance of the blood serum. From 5 to 6 c.c. are injected several times, however, not before the patient has recovered from the reaction following the preceding injection. From one to two hours after the injection the patient has chills and there is a rise in temperature—the height of which is attained within from ten to twelve hours. As to the blood, there is first leukopenia, then an increase of the leukocytes. This treatment is most successful in epididymitis, periurethritis, protaritis, gonorrhea, buboes and affections of articulation. No effect is seen on gonorrheic urethritis and soft chancres; it is also effective in the eczemas and trichophytosis.

ANAEROBIC CULTURES OF GONOCOCCI. Dr. Buschke.

Dr. Buschke of Berlin explained his experiences with anaerobic cultures of gonococci (on human serum). The gonococci can be preserved for a long time although they multiply slowly. Applying his experiences to the prognosis of chronic gonorrhea, his opinion is that in many cases of gonorrhea a latent infection exists, that is, gonococci remain hidden without showing clinical symptoms. Basing his arguments on the preference gonorrhea shows for the seminal vesicles, prostate gland, etc., as well as on our inability to get at latent gonococci, Buschke is pessimistic as to our chances of curing gonorrhea.

A long discussion followed in which Gennerich, Blaschko and others expressed more optimistic views.

GONORRHEIC ULCERS. Dr. Fuchs.

Dr. Fuchs said that gonorrheic ulcers are very superficial, not undermined, prone to bleed, and seldom found in women. A 10 per cent. solution of nitrate of silver destroys them.

GENESIS OF CARCINOMA CAUSED BY ARSENIC. Dr. Ullmann.

Dr. Ullmann of Vienna discussed the genesis of carcinoma caused by arsenic. The disease is practically limited to America and the British colonies on account of the high doses of arsenic given in these countries. Often furunculosis and hyperhidrosis are combined. Histologic examination showed a resemblance to ordinary carcinoma.

NEW NOMENCLATURE FOR DISEASES OF THE SKIN. Dr. Rost.

Dr. Rost of Freiburg proposed a new distinction and nomenclature for the diseases of the skin. He would like to see these diseases classified according to:

(*a*) Lesions (external causes).

1. Specific (bacilli, etc.).
2. Chemical.
3. Physical.

(*b*) Dispositions (internal causes).

1. Nutritive disorders.
2. Neurogenous disorders.
3. Vascular disorders.
4. Genetic disorders.

INFLUENCE OF INTRAVENOUS INJECTIONS OF SILVER ON GONORRHEA. Dr. Heucky.

Dr. Heucky of Munich discussed the influence of intravenous injections of silver on gonorrhea. His experiments show that little can be expected from this method in itself unless it is combined with local treatment. The combined method cured 72 per cent. of the cases of uncomplicated gonorrhea in females. The disadvantages of using injections of silver are that headaches and giddiness are sometimes caused; also the length of treatment, as very small doses only in increasing rising concentrations can be administered. In cases of epididymitis this treatment did not prove as effective as the vaccine therapy, whereas in prostatitis it gave better results than the latter. In vulvo vaginitis infantum the results were good. In a few cases Heucky cured gonorrhea in females with silver arsphenamin.

The congress was closed by a visit to the Hospital for Tropical Diseases. A large number of interesting cases of ulcus tropicum, oriental sore, sporotrichoses, etc., were demonstrated.

Edward Ahlswede, M.D., Hamburg, Germany.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, May 18, 1921

Barker B. Beeson, M.D., *Presiding*

FOLLICULITIS AND PIGMENTATION. Presented by Drs. Ormsby and Mitchell.

A man, aged 24 years, was under treatment for pruritus ani and was also being treated for syphilis by another physician. On his trunk were lesions which had been present, and in the same condition, for six or seven years, consisting of areas of pigmentation, small follicular papules and minute pustules. Itching had preceded the appearance of the dermatosis. The patient denied chancre and all secondary infections, and antisyphilitic treatment had had no effect on the skin lesions.

DISCUSSION

Dr. Foerster thought a more careful examination would be necessary before he could make a diagnosis. The multiformity of the lesions, together with the pustular folliculitis which had been followed by infiltration and later by atrophy, suggested tuberculids, although the lesions were not in the usual areas. He was unable to classify the disorder in any other group.

Dr. Senear believed tuberculid would have to be considered, but he was inclined to regard the condition as a case of chronic, low-grade folliculitis.

Dr. Lieberthal considered it a case of acne vulgaris.

Dr. Ormsby regarded the case as an unusual amount of pigmentation following follicular pus infections.

BLASTOMYCOSIS. Presented by Dr. Waugh.

A man, aged 38 years, whose disorder had been present for nine months, had two lesions, one covering over half of the nose and the other behind the lobe of the left ear. The lesion on the nose was distinctly papillomatous, bluish red, with some purulent secretion and a few pinhead size miliary abscesses near the margin. Blastomyces had been demonstrated microscopically. The patient had recently been discharged from the Municipal Tuberculosis Sanitarium, where he was treated for pulmonary tuberculosis.

DISCUSSION

Dr. Baer thought the lesions and the organisms demonstrated under the microscope were characteristic of blastomycosis.

Dr. Ormsby thought the diagnosis lay between tuberculosis and blastomycosis, and the only possible way to demonstrate the difference between the two conditions was by demonstration of the blastomyces. He was unable to accept the organism under the microscope as that of blastomycosis.

Dr. Waugh said he had thought of tuberculosis verrucosa cutis. The case resembled that disorder to some extent. The miliary abscesses in the margin of the lesion on the nose, however, were typical of blastomycosis. He had been able on previous occasions to demonstrate typical budding blastomyces. The sputum had not been examined, and it was possible that the patient had pulmonary blastomycosis as the tubercle bacillus had not been found when the patient was in the sanatorium.

DERMATITIS HERPETIFORMIS. Presented by Dr. Oliver.

A child, aged 1½ years, presented a disorder which had been present since March, 1921, when enlarged glands in the neck had been noted. The mother had influenza in March, 1919, while pregnant.

The lesions consisted of bullae, vesicles and papules and were grouped over the scalp, face, arms, back, buttocks, legs and face. Marked itching was present. The condition responded promptly to the administration of Fowler's solution.

DISCUSSION

Dr. Pusey thought it was a case of dermatitis herpetiformis.

Dr. Michelson thought it probably had been a case of multiform erythema, because of the rapid development and rapid involution of the lesions.

Dr. Oliver called attention to the fact that the mother had had influenza during the gestation of this child, and that the baby had always been nervous. He had considered the diagnosis of erythema multiforme on account of the multiform character of the lesions, but the intense itching, the grouping and the response to arsenical therapy led him to regard the case as one of dermatitis herpetiformis.

CASE FOR DIAGNOSIS. Presented by Dr. Senear.

A woman, aged 38 years, whose trouble began on the nose about five months ago, was seen at the University of Illinois in February, at which time the entire lower two thirds of the nose was bright red, enlarged, and presented a papillomatous appearance, with some discrete pustules. Tertiary syphilis, severe acne rosacea and blastomycosis had to be considered. Examination of the pus disclosed sporelike bodies, some of them budding. Despite the fact that neither the clinical picture nor the organisms were typical of blastomycosis, the patient was given potassium iodid, and the eruption cleared up within two or three weeks. Within a short time there was a recurrence, and the potassium iodid was then without effect. It was stopped after a short time as the condition seemed to become worse.

DISCUSSION

Dr. Foerster thought the case might have been one of blastomycosis at the onset, but that the lesions now looked like an ulcerated nodular syphilid.

Dr. Quinn agreed with Dr. Foerster.

Dr. Senear said he did not intend to give the impression that a diagnosis of blastomycosis had been made when the case was first seen. He was not sure about the organism under the microscope. The Wassermann reaction was negative. The present eruption had not responded to potassium iodid, and he was afraid to continue that drug because of the possibility of increasing the pustular element. No mercury or arsphenamin had been administered.

Dr. Pusey thought the lesions on the nose were probably not due to potassium iodid and believed mercury and potassium should be given a fair trial before abandoning the diagnosis of syphilis.

Dr. Ormsby stated that he saw this patient on one occasion in January, 1921. At that time he made a diagnosis of rosacea with an acute dermatitis due to the application of an irritating ointment. The patient was in a belligerent mood and was planning to sue a druggist for improperly filling a prescription. At the present time the lesions so closely resembled a syphilid that he felt there was no doubt about the diagnosis. He advised the use of arsphenamin.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by Drs. Ormsby and Mitchell.

A woman, aged 56 years, injured her hand in October, 1920, and later developed a lesion near the site of injury. Her son had recently died of pulmonary tuberculosis, and she had nursed him throughout his illness. The lesion began as a small nodule at the base of the right thumb, on the dorsal surface, and gradually enlarged. At the time of presentation this was a dollar-sized, well defined, slightly elevated, crusted, erythematous lesion. A

small crusted lesion was present on the flexor side of the wrist, and there were thickened patches on the left shin near the shoetop, which were said to have been present for years. The scalp was clear.

The patient was under treatment with roentgen therapy.

DISCUSSION

DR. PUSEY regarded the case as a beautiful example of tuberculosis verrucosa cutis.

DR. ORMSBY said the case was typical and thought it was interesting on account of the rapid progress of the infection.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

The patient was a man, aged 28 years, who was first shown before the society in 1917 by Dr. Harris. At the age of 3 years he had a bullous eruption which persisted until he was 16, when it disappeared. This disorder recurred a year and a half ago and has persisted since that time. The lesions were grouped, and itching was intense. In association with this he had developed a brownish desquamation in the axillary folds, the bends of the elbows, on the abdomen and elsewhere at points of friction or pressure. When shown in 1917 the patient presented only the latter type of lesion. Acanthosis nigricans and ichthyosis were considered as diagnoses at that time.

The previous report appeared in the *Journal of Cutaneous Diseases* **36**:245, 1918.

DISCUSSION

DR. ZEISLER regarded the case as one of dermatitis herpetiformis followed by pigmentation.

DR. PUSEY said that in his opinion it was not a simple pigmentation. In the axilla there were verrucous lesions and papillary hypertrophy. He was unable to accept the diagnosis of dermatitis herpetiformis with pigmentation, and believed the only condition which resembled it was acanthosis nigricans. He was beginning to believe that acanthosis nigricans was probably a loose sort of entity—concerning whose course there was a good deal to be learned; he recalled a case that he had demonstrated before the society twenty years ago, which had almost completely cleared up.

DR. FOERSTER said the skin was of the ichthyotic type about the ears, backs of the hands and arms, and believed it might be a case of ichthyosis hystrix with dermatitis herpetiformis.

DR. SENEAR said that when this patient was shown in 1917 he had had a period of freedom from the bullous manifestation of the disease for four years. He had seen the patient recently during an accute stage of the eruption. He had reconsidered the diagnosis of ichthyosis and acanthosis nigricans for the scaly and pigmented part of the eruption. The vesicular eruption comes on rapidly and involutes rapidly; the lesions are grouped and itch severely.

LICHEN PLANUS. Presented by DRS. ORMSBY and MITCHELL.

The patient was a practicing physician, aged 54 years. The first attack occurred eight years ago and cleared up with tar preparations. He remained free from the eruption for three years, when a less severe attack occurred which disappeared soon after the lesions had been cauterized. Three years ago he had had another severe attack which lasted only a few weeks and in

which the eruption had been cleared up by protiodid of mercury. The lesions were situated chiefly on the backs of the hands, with some on the legs and abdomen. For the last four or five months he had had lesions of the same areas, but also some of a different type. Two or three months ago small red patches of raised epidermis appeared here and there. These could be easily rubbed off, without scratching, and this was followed by bleeding. Large, confluent areas covered the greater part of the ulnar surface of both legs, and in these areas erosions had occurred in several places. Typical lichen planus papules were present on the forearms and scrotum, as well as on the buccal mucous membrane. Nikolsky's sign was present. The patient had diabetes and high blood pressure, and there was some anasarca of the legs.

DISCUSSION .

DR. BAER thought the lesions were typical of those of lichen planus.

DR. EISENSTAEDT said the lesions on the wrist were characteristic of lichen planus. The unusual feature of the case was the presence of Nikolsky's sign, which he had not noted heretofore in this disease.

DR. PUSEY thought that the ease with which the epidermis could be removed in this case amounted to the presence of Nikolsky's sign. He was unable to accept this as pathognomonic of pemphigus. Some years ago he saw the sign present in an erythematous and papular multiform erythema, and since he had observed it in a number of different dermatoses. He thought the explanation was, in this case as in others, that there was an exudation sufficient to produce a loosening of the corneous layer but not sufficient to produce the formation of vesicles. This was an instance of Nikolsky's sign in lichen planus.

DR. MICHELSON said he had seen two cases of lichen planus occurring in physicians, and in both instances the patients had resorted to irritating applications rather than to submit to intramuscular injections. He believed this case was probably similar to the ones he had seen, and that the external applications probably had injured the epidermis to the point of producing what appeared to be Nikolsky's sign.

DR. ORMSBY said that the patient was now receiving intramuscular injections of mercuric chlorid. He agreed with Dr. Pusey in regard to Nikolsky's sign. Some years ago he saw a patient with lichen planus who had bullous lesions on the legs, but he had taken no arsenic. In this case the lesions were not classic but abortive bullae.

LINGUA NIGRA. Presented by DR. WAUGH.

The patient was a colored man, aged 30 years. The disorder had been present for five months and involved most of the dorsal surface of the tongue. The condition of the anterior third of the involved area had been practically cleared up with radium treatment.

DISCUSSION

DR. SENEAR was much interested in the results obtained by the radium therapy.

DR. PUSEY was anxious to know whether the lesions removed by radium would recur. If they did recur, he thought the advisability of again removing them with radium was doubtful. He believed it would be better to have the lesions on the tongue than to produce radium changes in it.

DERMATITIS HERPETIFORMIS. Presented by Dr. Zeisler.

The patient was a boy, aged 12 years, whose disorder had been present for three years. The lesions were scattered over the scalp, face and body, and he was unable to sleep because of the intense itching and burning. Marked photophobia was present. At the time of presentation there were grouped macules and dried vesicles, which were situated chiefly on the trunk. The Wassermann test was negative. A blood count showed an eosinophilia of 8 per cent.

DISCUSSION

Dr. Baer agreed with the diagnosis of dermatitis herpetiformis but was unable to say what connection the photophobia might have with the dermatosis.

Dr. Foerster thought the presence of scleral and conjunctival lesions would account for the photophobia, and asked whether such lesions were present.

Dr. Zeisler said he had observed definite vesicles and wheals. The patient was receiving arsenic and was improving rapidly. The grouping of the lesions was a pronounced feature of the dermatosis.

LUPUS ERYTHEMATOSUS OF THE LIP. Presented by Dr. Lieberthal.

This patient was demonstrated at the January, 1921, meeting of the Chicago Dermatological Society (Arch. Dermat. & Syph. **3**:674 [May] 1921). At that time the reaction following radium therapy had not subsided. The patient was shown again to demonstrate the results of radium therapy.

SYRINGO-CYST ADENOMA. Presented by Drs. Ormsby and Mitchell.

The patient was a girl, aged 17 years, who had had the disorder for about four years. It began in the fall as what she thought was "prickly heat," and had not spread since first noticed.

The lesions were grouped on the sides of the neck and upper chest and consisted of round and oval, light brown, slightly elevated match-head to pea-sized nodules, about 100 in all. This area sometimes becomes very red; itching occurs periodically and is intense for a minute or two. Dermographism was slight.

DISCUSSION

Dr. Pusey said he now had a patient with lesions similar to these. The clinical picture and the sections in his case constituted a replica of the case reported by White.

Dr. Foerster believed this disorder is probably much more frequent than the number of cases reported would indicate. He had often seen single discrete lesions in patients under examination for other disorders.

Dr. Lieberthal said he demonstrated a typical case before the society several years ago, but the microscopic picture was not that of a syringo-cyst adenoma, and there were none of the characteristic findings of that disorder present.

Dr. Senear wished to know whether radiotherapy was giving results in this case. The late Dr. Shaffner had obtained such excellent results from this method of treatment in the case he showed several years ago. In the first biopsy made in their case only a few adenomas were shown, but in the subsequent biopsy they found the characteristic changes.

Dr. Ormsby said that in this case the clinical diagnosis had been made when the patient was first seen. No attempt had been made to secure a biopsy because of the disposition of the patient. The case differed from the one he reported some years previously under the title syringoma in that the lesions in that case were extensive and the sweat function had entirely ceased. The lesions subsequently cleared up and sweating was restored. The histology in that case showed what appeared to be typical benign epithelioma. There was marked epithelial hypertrophy of the coils. The patient recovered entirely after the use of roentgen therapy.

FOLLICULITIS DECALVANS. Presented by Dr. Oliver.

A man, aged 26 years, presented lesions in the scalp which began in October, 1912, and which had persisted despite treatment ever since. Papules, papulo-pustules and considerable alopecia were present. He complained of itching and burning.

DISCUSSION

Dr. Lieberthal had first thought of favus in this case. The patient was American born of Polish parents and, therefore, might have acquired the disease from Polish born relatives or friends. The lesions were not typical of favus but were sufficiently suggestive to warrant search for the achorion. He believed the diagnosis lay between favus and folliculitis decalvans, with the probability of the latter being the correct one.

Dr. Foerster found that the scars were granular and not smooth and depressed as in favus. He felt quite sure the case was one of folliculitis decalvans.

Dr. Oliver was glad to have the suggestion in regard to favus and said he would make a careful examination for the achorion. He regarded the case as one of folliculitis decalvans.

A CASE FOR DIAGNOSIS. Presented by Dr. Senear.

The patient was a girl, aged 17 years, who complained of redness of the face which had been present for about eight months. It was said to have developed over night.

The cheeks showed a diffuse, sharply outlined erythema, covered with very fine, adherent scales. Soothing applications had been used locally without effect.

DISCUSSION

Dr. Pusey said the symmetry, the scaling and a slight increase in the thickness of the skin in the areas involved suggested a superficial lupus erythematosus.

Dr. Lieberthal agreed with Dr. Pusey's diagnosis. He thought the description of erythema centrifugum fitted the case—a diffuse form of the disease.

Dr. Senear was struck by the close resemblance of the face in this case to that in the man who was shown with lupus erythematosus by Dr. Waugh. He had not observed the atrophy in the lesions until it was pointed out to him by Dr. Foerster. He agreed with the diagnosis of Dr. Pusey.

LICHEN PLANUS HYPERTROPHICUS. Presented by Dr. Zeisler.

The patient, a man aged 42 years, had had the lesion on the internal surface of the right leg for two years. He worked with cyanid of potassium, to which he attributed the disorder.

The lesions occupied the entire inner surface of the right leg from the knee to the ankle. They were confluent, shiny, purplish-red, somewhat verrucous plaques. Intense itching was present.

DISCUSSION

DR. QUINN was unable to make a diagnosis.

DR. PUSEY said it was a queer case of a queer disease; namely, lichen planus.

DR. ZEISLER agreed with Dr. Pusey.

A CASE FOR DIAGNOSIS. Presented by DRS. ORMSBY and MITCHELL.

The patient was a man, aged 39 years, whose trouble began in September, 1917, as blisters on the abdomen about the belt line. Other lesions appeared later on the nose and ears and in the scalp, and scattered over the body, grouped between the shoulders. Remissions had occurred, but the disorder had never entirely cleared up. No vesicles had been seen, but Nikolsky's sign has been constantly present. Crusting had been present since the time of onset. No subjective sensations were present. One brother had had pulmonary tuberculosis. Exacerbations of rather severe character had occurred twice yearly in spite of treatment. All blood examinations had been negative. No biopsy had been made.

DISCUSSION

DR. FOERSTER thought the duration of three and a half years, the lack of response to treatment and the peculiar uniformity of the lesions suggested a benign form of pemphigus.

DR. PUSEY summarized the salient features of the case as follows: The man had a patch on the nose which was red and almost weeping, and there were numerous seborrheic patches on the forehead. He also had a great deal of dandruff of the scalp. He thought Hebra's form of lupus erythemtosus, which Hebra called seborrhea congestiva, fitted the picture in this case. He was unable to see how one could get away from that diagnosis. The duration and lack of response to treatment suggested lupus erythematosus. He was not ready to offer a diagnosis as to the patches on the body.

DR. LIEBERTHAL thought the greasy character of the patches suggested the diagnosis of seborrhea, and believed that the appearance of the lesion over the nose and cheeks might be in part due to external applications.

DR. ORMSBY said that when the patient was first seen there were crusted lesions on the chest and back. At that time there were only a few lesions on the nose, but gradually and almost imperceptibly the lesions spread. The erythematous condition of the lesions now was probably in part due to the recent removal of the crust by the use of ointment. The patient had received intensive internal treatment with mercury and arsenic, but the disorder had progressed in spite of the internal and external treatment. The patient stated that he had vesicles from time to time, but Dr. Ormsby had never been able to find them. The case was different from any he had hitherto seen. The description of lupus erythematosus on the face fitted the lesions exactly. The lesions on the body had resembled seborrheic dermatitis, but salicylic and sulphur ointment was without any appreciable effect. The disorder had the therapeutic rebelliousness of lupus erythematosus and the appearance of seborrheic dermatitis.

A CASE FOR DIAGNOSIS. Presented by Dr. Oliver.

The patient was a colored man, aged 25 years, who had lesions on the tongue which had been present for the past four months. They were not painful and had been little influenced by treatment. The patient had had a chancre four years ago. He had recently received five injections of neo-arsphenamin. The Wassermann reaction was negative.

DISCUSSION

Dr. Baer considered this case one of geographic tongue.

Dr. Lieberthal agreed with Dr. Baer.

Dr. Quinn also agreed with Dr. Baer.

Dr. Ormsby thought the lesions were multiple benign plaques, and said he had treated a number of such cases with radium with excellent results.

Book Reviews

DERMATOLOGY. THE ESSENTIALS OF CUTANEOUS MEDICINE. By WALTER JAMES HIGHMAN, M.D. Cloth. Price, $6. Pp. 482, with 95 illustrations. New York: Macmillan Company, 1921.

Highman states in his preface that another reference book of dermatology would have no justification, and that his volume "aims to present essentials succintly, consecutively, completely and simply, without sacrificing important detail." The contents therefore include "the author's conception of the minimum requisite for an adequate outline of the subject." In addition he has attempted to handle the subject, "so far as practicable, from the standpoint of internal medicine" emphasizing the beliefs connected with the interrelation of skin diseases and internal medicine.

It is true that with so many excellent texts of dermatology already available, a new treatise should have some special features to justify its existence, and it seems to the reviewer that Highman's text meets this requirement. Bibliography, histologic descriptions, and historical sketches, all of importance in the larger reference books, have been sacrificed in order to present to the novice or general practitioner only those things which are essential. The descriptions of the symptoms of the various diseases deal chiefly only with the characteristic pictures, although the variations are never slighted, but mentioned briefly—usually in fine print. The sections on differential diagnosis are excellent, the various differenital points being detailed so fully as to be of great value to the inexperienced.

The discussion on etiology and pathogenesis, while complete, dismisses many theories with a word, but gives fully those which have impressed the author as being important. It is in these discussions that particular attention has been given to the inter-relation of dermatoses and the physical economy as a whole, and Highman presents clearly the pros and cons of the various theories.

In discussing the treatment of the various disorders, the author includes only those methods which have commended themselves to him. The reader has, therefore, no large list of therapeutic aids to select from, but those given are well chosen, furnish an adequate armamentarium, and their value is greatly enhanced by the frequent detailed discussion of their indications and the methods of employing them.

A valuable feature of the book is the frequent use of classifications, giving the reader a survey of the clinical or etiologic relationships of many diseases; the chart of nevi on page 354, and that of multicellular animal parasites on page 223 are illustrations of this.

In following out his policy of giving special attention to internal medicine, Highman has included a comprehensive section dealing with the cutaneous manifestation accompanying various general disorders, such as typhoid, typhus, pertussis, mumps, etc.

The illustrations, while they number only ninety-five, are all in plate form, and are selected to illustrate well the more common cutaneous disorders. The legends accompanying the illustrations are detailed, usually giving a short résumé of the main points in the condition pictured, and pointing out those features which are illustrated. In one instance the text and the legend do not agree, however, as in discussing pompholyx he states that it is "associated with

a disturbance of the sweat secretion," while the legend of Figure 16 states that "there is no real association with sweat disturbance."

The book is replete with expressions of the author's opinions on many points, and while not all will agree that pityriasis rosea "is clearly infectious," that dermatitis herpetiformis and pemphigus are so closely related as possibly to destroy the former as a clinical entity, etc., it is always made clear that these are disputed points. The discussion of the questionable duality of eczema and simple dermatitis, that of the term "precancerous" and other topics serve to show the usual decisive opinions of the author.

The text can be recommended to the beginner and those inexperienced in dermatology—for whom the author states that it was intended—as a valuable aid in the recognition and treatment of cutaneous diseases, while it will help them to understand more clearly that dermatoses are frequently only the outward expressions of more general disorders. Those more experienced in dermatology will also find much to interest them in the up-to-date exposition of this aspect of their specialty.

AN ATLAS OF THE PRIMARY AND CUTANEOUS LESIONS OF ACQUIRED SYPHILIS IN THE MALE. By CHARLES F. WHITE, O.B.E., M.B., Major, Royal Army Medical Corps; Lecturer on Venereal Diseases and Officer in Charge of the Rochester Row Military Hospital; and W. HERBERT BROWN, M.D., Physician for Diseases of the Skin, Victoria Infirmary, Glasgow; Late Captain, Royal Army Medical Corps (T.C.); with a Foreword by LIEUT.-GEN. SIR T. H. J. C. GOODWIN, K.C.B., C.M.G., D.S.O., K.H.P., Director-General, Army Medical Service. New York: William Wood and Company. 1920.

This small quarto with thirty-three pages of text, seventy-nine illustrations in black and white and about twenty illustrations in color is an effort to salvage some of the extensive experience in venereal diseases obtained in a large army hospital during the war. Its production represents a commendable spirit, and one approaches the book with predilections in its favor. The text, while brief is clear, concise and comprehensive. The authors have succeeded well in the brief space at their disposal in summarizing a great experience. The illustrations in color, while not numerous, are good. Neither the English nor we are as yet able to produce as good colored pictures as are produced in continental Europe, particularly in Germany, but these colored pictures are well up to the best standard of English or American production. Some imperfection in the coloring of the colored pictures is not a great defect in the reviewer's estimation, for colored pictures are not as useful as black and white illustrations of skin diseases unless they represent the colors perfectly, and that is excessively rare. The halftones made from photographs are excellent. They are well selected, illustrate most of the manifestations of syphilis of the surface, and are sharp and clear. The photographs are all stereoscopic and are produced in duplicate, and, examined with a stereoscope, they show the lesions remarkably well.

The one criticism to be made of the book is the price—$9.00. The prices of English books at present are often excessive. This monograph is a well illustrated chapter on cutaneous syphilis. Except for the stereoscopic feature, these illustrations are no better and are not much more numerous than will be found in articles on syphilis in standard works. Nine dollars is too large a price for such a production.

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